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Cover Page

CLINICAL INVESTIGATIONAL PLAN

EMINENT

A randomized trial comparing the ELUVIA™ drug-eluting stent versus bare Metal self-expanding nitINol stEnts in the treatmeNt of superficial femoral and/or proximal popliteal arTeries

NCT Number: 02921230

CIP nr: S2366

VERSION: 3.0

DATE: 23 December 2019

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This protocol contains confidential information for use by the Investigators and their designated representatives participating in this clinical investigation. The protocol should be held confidential and maintained in a secure location.

Sponsored By:

Boston Scientific International SA

Le Val Saint Quentin
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France

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Study Title	A randomized trial comparing the ELUVIA™ drug-eluting stent versus bare Metal self-expanding nitINol stEnts in the treatmeNt of superficial femoral and/or proximal popliteal arTeries **(EMINENT)**
CIP Number	S2366
CIP Version	3.0
CIP Date	23 December 2019

Prof. Dr. Giovanni Torsello Coordinating Clinical Investigator	Date
Prof. Dr. Yann Goueffic Coordinating Clinical Investigator	Date
Andrew Campbell Clinical Trial Manager Sponsor representative	Date

2. CIP SIGNATURE PAGE

Study Title	A randomized trial comparing the ELUVIA™ drug-eluting stent versus bare Metal self-expanding nitINol stEnts in the treatmeNt of superficial femoral and/or proximal popliteal arTeries **(EMINENT)**
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I have reviewed this protocol and agree to adhere to the requirements and responsibilities listed herein. I am trained to the contents of this protocol, percutaneous angioplasty procedures, and the specific use of the devices listed in this protocol. I will ensure that the study is conducted in compliance with the protocol, Good Clinical Practices, Declaration of Helsinki, the International Standard ISO 14155:2011 and all applicable regulatory requirements.

_____ _____

Site Principal Investigator Name (please print or use stamp) Site Number

_____ _____

Site Principal Investigator Signature Date

3. CIP EXECUTIVE SUMMARY

PROTOCOL TITLE: A randomized trial comparing the ELUVIA™ drug-eluting stent versus bare Metal self-expanding nitINol stEnts in the treatmeNt of superficial femoral and/or proximal popliteal arTeries **(EMINENT)**

CIP Short title	EMINENT
CIP number	S2366
Sponsor	Boston Scientific International SA
Objective	To confirm the superior effectiveness of the ELUVIA Drug-Eluting Vascular Stent System (ELUVIA Stent) for treating Superficial Femoral Artery (SFA) and/or Proximal Popliteal Artery (PPA) lesions up to 210 mm in length when compared against bare metal stents, and collect additional data including health economics data.
Planned Indication(s) for Use	The ELUVIA Stent System is intended to improve luminal diameter in the treatment of symptomatic de novo or restenotic lesions in the native SFA and/or PPA with reference vessel diameters (RVD) ranging from 4.0-6.0 mm and total lesion lengths up to 210 mm.
Test Device	The ELUVIA Stent is a paclitaxel-eluting, self-expanding nitinol stent developed on the same stent and delivery system as the BSC Innova™ Vascular Self-Expanding Stent System.
Control Device	Commercially available stents in Europe. Permitted stents are Supera (Abbott), Lifestent (CR Bard), Everflex (Covidien/Medtronic), S.M.A.R.T. Flex (Cordis/Cardinal), S.M.A.R.T. Control (Cordis/Cardinal), Pulsar (Biotronik), COMPLETE SE (Medtronic), Misago (Terumo) or Innova (Boston Scientific) indicated for improving luminal diameter for the treatment of *de novo* or restenotic symptomatic lesions in native vascular disease of the above-the-knee femoropopliteal arteries.

<table>
<tr><td>Device Sizes</td><td>ELUVIA Stent (Test Device)
<table>
<tr><th>Stent Diameter (mm)</th><th>Stent Length (mm)</th><th>Recommended Vessel Diameter (mm)</th></tr>
<tr><td>6</td><td>40, 60, 80, 100, 120, 150</td><td>4.0 – 5.0</td></tr>
<tr><td>7</td><td>40, 60, 80, 100, 120, 150</td><td>5.0 – 6.0</td></tr>
</table>
The ELUVIA Stent is available in two stent delivery system (SDS) sizes; 75 cm and 130 cm. The sheath compatibility is 6 French used with 0.035 inch guidewires.

Self-Expanding Stents - Bare Nitinol (Control Devices)

Permitted stents are Supera (Abbott), Lifestent (CR Bard), Everflex (Covidien/Medtronic), S.M.A.R.T. Flex (Cordis/Cardinal), S.M.A.R.T. Control (Cordis/Cardinal), Pulsar (Biotronik), COMPLETE SE (Medtronic), Misago (Terumo) or Innova (Boston Scientific).</td></tr>
<tr><td>Study Design</td><td>A prospective, multi-center study confirming the superior effectiveness of the ELUVIA stent versus Self-Expanding Bare Nitinol Stents in the treatment of lesions 30-210 mm long located in the femoropopliteal arteries in subjects with symptoms classified as Rutherford categories 2-4.

The study is a 2:1 randomized (ELUVIA vs Self-Expanding Bare Nitinol Stents), controlled, single-blind, superiority trial (RCT). Randomization will be stratified to ensure equal distribution of ELUVIA and Self-Expanding Bare Nitinol Stents in different lesion length subsets.</td></tr>
<tr><td>Primary Endpoint</td><td><u>Primary Effectiveness Endpoint</u>

The primary effectiveness endpoint assesses primary patency at 12 months post-procedure. This effectiveness endpoint is designed to demonstrate that the 12-month primary patency for the ELUVIA treatment group is superior to the Self-Expanding Bare Nitinol Stents treatment group.

Primary vessel patency is defined as a binary endpoint and will be determined to be a success when the duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) is ≤ 2.4 at the 12-month follow-up visit in the absence of clinically-driven TLR or bypass of the target lesion. All DUS readings will be assessed by an independent core laboratory</td></tr>
</table>

Secondary Endpoint	Health-Economics - Walking Improvement at 12 months assessed by change in Six Minute Hall Walk (6MHW) / treadmill test from baseline, or preceding any Target Vessel Revascularization - Walking Improvement at 12 months assessed by change in Walking Impairment Questionnaire (WIQ) from baseline - Quality of Life Improvement at 12 months assessed by change in EQ-5D-5L™ from baseline, or preceding any Target Vessel Revascularization - Cost effectiveness of ELUVIA™ drug-eluting stent versus bare metal self-expanding nitinol stents - Rate of Primary and Secondary Sustained Clinical Improvement at 12 months as assessed by changes in Rutherford Classification from baseline - Rate of Hemodynamic Improvement at 12 months as assessed by changes in Ankle-Brachial Index (ABI) from baseline
Additional Endpoints	- Technical success - Procedural success - Major Adverse Event (MAE) rate (and individual components) at each time point, defined as all causes of death, target limb major amputation and/or Target Lesion Revascularization (TLR) - Primary Patency and Assisted Primary Patency at 6 months, 12 months, 24 months and 36 months using different DUS PSVRs - Clinically-driven TLR and clinically-driven Target Vessel Revascularization (TVR) Rate at each time point - Adverse Event Rates (unanticipated, major, serious, device/procedure-related) at each time point - Survival rate at 4 years and 5 years post-procedure - Number of Stent Fractures reported at 12 months and 24 months utilizing VIVA definitions - Distribution of Rutherford Class during follow-up as compared to baseline at 1 month, 6 months, 12 months, 24 months and 36 months - Walking Improvement at 1 month, 6 months, 24 months and 36 months assessed by change in Walking Impairment Questionnaire (WIQ) from baseline - Quality of Life Improvement at 1 month, 6 months, 24 months and 36 months assessed by change in EQ-5D-5L™ from baseline - Rate of Primary and Secondary Sustained Clinical Improvement as assessed by changes in Rutherford Classification from baseline at 1 month, 6 months, 24 months and 36 months - Rate of Hemodynamic Improvement as assessed by changes in Ankle-Brachial Index (ABI) from baseline at 1 month, 6 months, 24 months and 36 months

Population	750 subjects to receive treatment with either the test device (ELUVIA, N=500 subjects) or a control device (Self-Expanding Bare Nitinol Stents, N=250 subjects). Up to 75 study centers in up to 15 European countries may enroll subjects in the study.
Study Duration	It is expected that the enrolment will take approximately 18 months. The study will be considered complete (with regard to the primary endpoint) after all subjects have completed the 12 month follow-up visit, were discontinued prior to the 12 month follow-up visit, have died, or the last 12 month follow-up visit window is closed. Subject participation will last approximately 5 years, including time required for screening. The trial will be considered complete (with regard to all follow-up) after all subjects have completed the 60 month (5 year) follow-up visit, were discontinued prior to the 60 month (5 year) follow-up visit, have died, or the last 60 month (5 year) follow-up visit window is closed. It is estimated that it will take approximately 8 years to complete this trial.
Inclusion Criteria	1. Subjects age 18 and older 2. Subject is willing and able to provide consent before any study-specific test or procedure is performed, signs the consent form, and agrees to attend all required follow-up visits 3. Chronic, symptomatic lower limb ischemia defined as Rutherford categories 2, 3 or 4 4. Stenotic, restenotic or occlusive lesion(s) located in the native SFA and/or PPA: a. Degree of stenosis ≥70% by visual angiographic assessment b. Vessel diameter ≥ 4 and ≤6 mm c. Total lesion length (or series of lesions) ≥ 30 mm and ≤ 210 mm (Note: Lesion segment(s) must be fully covered with one or two overlapping ELUVIA stent(s) or Self Expanding Bare Nitinol stent(s)) d. For occluded lesions (chronic occlusions) requiring use of re-entry device, lesion length ≤ 180 mm e. Target lesion located at least three centimeters above the inferior edge of the femur 5. Patent infrapopliteal and popliteal artery, i.e., single vessel runoff or better with at least one of three vessels patent (<50% stenosis) to the ankle or foot with no planned intervention

Exclusion Criteria	1. Previously stented target lesion/vessel 2. Target lesion/vessel previously treated with drug-coated balloon <12 months prior to randomization/enrollment 3. Subjects who have undergone prior surgery of the SFA/PPA in the target limb to treat atherosclerotic disease 4. Use of atherectomy, laser or other debulking devices such as Rotarex in the target limb SFA/PPA during the index procedure 5. History of major amputation in the target limb 6. Documented life expectancy less than 24 months due to other medical co-morbid condition(s) that could limit the subject's ability to participate in the clinical study, limit the subject's compliance with the follow-up requirements, or impact the scientific integrity of the clinical study 7. Known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated 8. Known hypersensitivity/allergy to the stent system or protocol related therapies (e.g., nitinol, paclitaxel, or structurally related compounds, polymer or individual components, and antiplatelet, anticoagulant, thrombolytic medications) 9. Platelet count <80,000 mm^3 or >600,000 mm^3 or history of bleeding diathesis 10. Concomitant renal failure with a serum creatinine >2.0 mg/dL 11. Receiving dialysis or immunosuppressant therapy 12. History of myocardial infarction (MI) or stroke/cerebrovascular accident (CVA) within 6 months prior to randomization/enrollment 13. Unstable angina pectoris at the time of randomization/enrollment 14. Pregnant, breast feeding, or plan to become pregnant in the next 5 years 15. Current participation in an investigational drug or device clinical study that has not completed the primary endpoint at the time of randomization/ enrollment or that clinically interferes with the current study endpoints (Note: studies requiring extended follow-up for products that were investigational, but have become commercially available since then are not considered investigational studies) 16. Septicemia at the time of randomization/enrollment 17. Presence of other hemodynamically significant outflow lesions in the target limb requiring intervention at the time of the index procedure 18. Presence of aneurysm in the target vessel 19. Acute ischemia and/or acute thrombosis of the SFA/PPA prior to randomization/enrollment.

	20. Perforated vessel as evidenced by extravasation of contrast media prior to randomization/enrollment. 21. Heavily calcified lesions. 22. As applicable by French law, subject who is a protected individual such as an incompetent adult or incarcerated person.
Method of Assigning Subjects to Treatment	Once the subject has signed the approved study Informed Consent Form (ICF), and has met all clinical inclusion and no clinical exclusion criteria, the subject will be considered eligible to be enrolled in the study. If the subject is found to meet exclusion criteria during the angiographic eligibility assessment, the subject will be considered a screen failure and should not be randomized and included in the study, nor should the subject be followed post-procedure per protocol. If the subject is found to meet the inclusion criteria during the angiographic phase of the procedure, the subject will be considered eligible to be randomized (2:1 allocation treatment versus control). Randomization will be stratified by lesion length (i.e. ≤110 mm vs. >110 mm) for each site. After the Investigator successfully crosses the target lesion with the guidewire, a randomization custom function within the eCapture electronic data capture (EDC) database will be used to assign subjects to the test or control treatment group. Subjects will be considered enrolled after they have been successfully randomized (i.e. when a treatment assignment is received by the study site).
Blinding/ Unblinding	The EMINENT study is a single-blind study. Subjects will be blinded to treatment assigned and treatment received. All subjects must remain blinded until completion of all 12-month follow-up visits (primary endpoint). Packaging of the test and control devices are different, therefore the investigator performing the procedure will not be blinded to the assigned treatment arm or resulting treatment. Study center personnel will be trained not to disclose the treatment assignment to the subject to minimize the potential unblinding of the subject. Site personnel conducting clinical follow-up will be blinded to a subject's treatment assignment whenever possible, and must remain blinded until completion of all 12-month follow-up visits (primary endpoint). Duplex Ultrasound Core Laboratory personnel, Angiography Core Laboratory personnel and the Clinical Events Committee (CEC) will be blinded to a subject's treatment assignment during the study. Those involved in data analysis for the Sponsor will remain blinded until the primary endpoint analysis. Instructions regarding the unblinding of a subject for a medical emergency can be found in the Unblinding guidelines.

Follow-up Schedule	All subjects will be evaluated at 6 (182 ±30 days), , 12 (365 ±30 days), 24 (730 ±30 days), 36 (1095 ±30 days), 48 (1460 ±90 days) and 60 (1825 -90/+30 days) months post-procedure. Subjects will be evaluated at 1 (30 days -7 days to + 14 days) month if visit is local standard of care or if an ELUVIA stent or Self Expanding Bare Nitinol stent was not successfully implanted during the Index Procedure. • Subjects who are randomized but an ELUVIA stent or Self Expanding Bare Nitinol stent was not successfully implanted will be followed through the 1-month follow-up visit only. Data for assessment of MAE will be collected for these subjects; other testing is not required. • Assessment of the primary effectiveness endpoint and secondary health-economics endpoint will occur at the 12-month follow-up visit. • All follow-up visits through 36 months will be conducted in the office/clinic. • Telephone follow-up visit at 48 months and 60 months post-procedure, and/or medical chart review and/or publicly available records consultation, if necessary. Planned protocol-required testing includes the following: • Angiography during the index procedure, and during any subsequent revascularization procedure, to assess technical success and procedural success. • DUS at 6 months, 12 months (1 year), 24 months (2 years), and 36 months (3 years) visits to assess lesion and vessel patency. • X-rays at 12 months (1 year) and 24 months (2 years) visits to assess stent integrity will be collected if performed per standard of care. • Walking Impairment Questionnaire (WIQ) at 1 month, 6 months, 12 months (1 year), 24 months (2 years), and 36 months (3 years) visits to assess Walking Ability • EQ-5D-5L™ at 1 month, 6 months, 12 months (1 year), 24 months (2 years), and 36 months (3 years) visits to assess Quality of Life In case a subject undergoes a re-intervention of the target vessel, it is recommended to perform a walking test (6MWT or treadmill test) and QoL questionnaire (EQ-5D-5L™) prior to the Target Vessel Revascularization.
Required Medication Therapy	Investigators must prescribe concomitant anti-coagulant and anti-platelet medications consistent with current local clinical practice. Antiplatelet medication usage will be collected and reported for the duration of the trial.
Multiple Interventions Using Same Access Site	Iliac lesion(s) in both limbs may be treated during the index procedure. Iliac lesions in the target limb should be treated ***prior to*** the target SFA/PPA lesion with commercially available devices (non-drug-eluting in the target limb)

During Index Procedure	and treatment must be considered successful (i.e. residual stenosis <30% and no clinical events [embolization, perforation]) Tandem lesions in the SFA/PPA may be treated during the index procedure, provided that the tandem lesions segment is ≤210 mm and can be covered with one or two overlapping ELUVIA stent(s) or Self Expanding Bare Nitinol Stent(s) according to each device's Instructions for Use (IFU/DFU). (Refer to Inclusion criterion 4c.) If an additional stent is required due to complications (e.g., dissection, misplacement or under-sizing of the target lesion), the additional stent(s) placed should be of the same type used to treat the target lesion.
Statistical Methods	Primary Effectiveness Statistical Hypothesis The primary effectiveness hypothesis to be tested is that the 12-month primary patency in subjects treated with ELUVIA is superior to subjects treated with Self Expanding Bare Nitinol Stents at one-sided significance level of 2.5%. Primary Effectiveness Statistical Test Method The Chi-Square Test will be used to assess the hypothesis of superiority in proportions: H_0: Pt - Pc ≤ 0 H_1: Pt - Pc > 0 (superior) where Pt and Pc are the 12-month primary patency for the ELUVIA (test) and Self Expanding Bare Nitinol Stents (control) groups, respectively. Secondary Health-Economics endpoint No formal tests of hypotheses are proposed for the secondary endpoint. Statistical comparisons may be performed for exploratory purposes.
Success Criteria	Success Criteria for Primary Effectiveness Endpoint ELUVIA will be concluded to be superior to Self-Expanding Bare Nitinol Stents for device effectiveness if the one-sided lower 97.5% confidence bound on the difference between treatment groups (ELUVIA – Self Expanding Bare Nitinol Stents) in 12-month primary patency is greater than zero. Success Criteria for the Study If the primary effectiveness endpoint is met, the RCT will be considered a success.

Sample Size Parameters	The primary effectiveness endpoint drives the overall sample size. <u>Primary Effectiveness Endpoint</u> • Power ≥ 85% • One-sided significance level (alpha) = 2.5% • To demonstrate 10%* treatment effect in effectiveness: • Expected ELUVIA 12-month primary patency = 85% • Expected Self Expanding Bare Nitinol Stents 12-month primary patency = 75% • Allocation (ELUVIA vs. Self-Expanding Bare Nitinol Stents) = 2:1 • Attrition rate in 12 months ≤ 16% • A minimum of 630 evaluable subjects are required at 12 months (ideally 420 ELUVIA, 210 Self Expanding Bare Nitinol Stents) • Approximately 750 subjects are planned to be randomized in a 2:1 fashion at enrollment *The 10% treatment effect represents 7% observed advance. Assuming a 12-month primary patency of 75.2% (158/210) is observed for Self Expanding Bare Nitinol Stents, a minimum of 82.1% (345/420) for ELUVIA will be required to claim superiority.

4. ASSESSMENT AND FOLLOW-UP SCHEME

Procedure/Assessment	Pre-procedure[3]	During Index Procedure	Pre-Discharge	1 MFU[10] (30 -7 days to + 14 days)	6 MFU (182±30 days)	12 MFU (365±30 days)	24 MFU (730±30 days)	36 MFU (1095±30 days)	48MFU [11] (1460 ± 90 days)	60 MFU [11] (1825 -90 / +30 days)	Prior to TVR
Informed Consent[1]	X										
In/exclusion criteria	X	X									
Demographics & Medical History	X										
Laboratory[2]	X										
Pregnancy test[3]	X										
ABI	X			X[4]	X	X	X	X			
RCC (Rutherford-Becker clinical classification)	X			X	X	X	X	X			
WIQ	X			X	X	X	X	X			
EQ-5D-5L	X			X	X	X	X	X			X[9]
6MHW or treadmill[8]	X					X[8]					X[9]
Angiogram[5]		X									
Randomization		X									
DUS[5]					X	X	X	X			
X-Ray[6]						X[6]	X[6]				
Health Economics				X	X	X	X	X			
Medication	X	X	X	X	X	X	X	X			X
Adverse Events[7]		X	X	X	X	X	X	X	X	X	X

1. Subject's consent may be obtained outside the 30 day window leading up to the procedure however, subject's consent and informed consent form must be signed prior to any study-specific tests or procedures
2. Serum Creatinine and Platelet Count to be measured
3. Performed within 30 days of procedure, except informed consent and except urine or blood pregnancy test required for females of childbearing potential performed within 7 days of procedure
4. ABI measurement may be collected immediately post-procedure through 1 Month Follow-up window (Day 0 – 44)
5. Angiograms and DUS will be sent to the respective core lab for analysis. Follow-up ultrasounds will not be required for any subject who underwent bypass surgery of the target lesion during the 36-month follow-up timeframe, or has a documented occluded stent.
6. X-ray only to be performed if per standard of care. If X-ray is done, images to be sent to the core lab for analysis.
7. Reporting required through the end of study for Major Adverse Events, UADEs, and (S)ADEs/Device Deficiencies.
8. Pre-procedure and at 12MFU, either 6MWT or treadmill can be performed, whatever is standard of care.
9. In case a subject undergoes a re-intervention of the target vessel, it is recommended to perform a walking test (6MWT or treadmill test) and QoL questionnaire (EQ-5D-5L™) prior to the TVR
10. The 1 month visit is only required if the visit is local standard of care or if an ELUVIA stent or Self Expanding Bare Nitinol stent was not successfully implanted during the index procedure.
11. The 48 month and 60 month visit will be conducted via telephone and/or medical chart review and/or publicly available records consultation.

5. CONTACT DETAILS

Contact information is provided below. This information is subject to change during the course of the clinical study. Periodic updates to study contact information will be sent to the sites and committees as needed.

Coordinating investigators	Prof. Dr. Giovanni Torsello Sint-Franziskus-Hospital GmbH Hohenzollernring 72 48145 Münster, Germany Prof. Dr. Yann Goueffic Hôpital Paris St Joseph, department of vascular and endovascular surgery 185 Rue Raymond Losserand, Paris, 75014-France
Sponsor	**Boston Scientific International SA** Le Val Saint Quentin 2 Rue René Caudron 78960 Voisins-Le-Bretonneux France
Clinical contact	**Andrew Campbell** Boston Scientific, Peripheral Interventions, Clinical Three Scimed Place Maple Grove, MN USA Andrew.Campbell@bsci.com
Investigational Sites	A list of investigational sites is maintained by the sponsor.
Vendors/labs	A list of vendors/labs involved in the trial is maintained by the sponsor.

6. INTRODUCTION AND RATIONALE

Peripheral Arterial Disease (PAD) is the third leading cause of cardiovascular morbidity after myocardial infarction (MI) and stroke. Current estimates state that there are over 200 million global patients with PAD[1,2] with an age–adjusted prevalence ranging from 12 to 20 percent.[3,4] Less than twenty percent of patients with PAD have typical symptoms of intermittent claudication such as leg muscle discomfort on exertion that is relieved by rest, or critical limb ischemia (CLI) (i.e., rest pain, ulceration or gangrene); whereas, another third have atypical

exertional leg symptoms. Notably, the risk of cardiovascular morbidity and mortality is equally high in patients with PAD, regardless of the presence of symptoms.[5] Non-revascularized lower extremity PAD is the most common cause of lower extremity amputation.[6]

6.1 Endovascular Treatment in SFA/PPA

In general, the debate for state-of-the-art therapy in SFA disease involves endovascular intervention versus bypass surgery. Historically, surgery is generally reserved for resting pain and critical limb ischemia. However, surgical therapy carries significant morbidity, including wound infection, MI and even death. In addition, up to 17 percent of the post-bypass surgery patients do not experience satisfactory clinical improvement.[7] Over the past decade, percutaneous catheter-based techniques have improved such that acute procedural success is high even in complex anatomy. Patency rates have also increased with the use of atherectomy devices and drug-eluting stents (DES). Often, patients with PAD have comorbidities that increase the risk of cardiovascular complications with surgical procedures. These factors have led to the adoption of an endovascular first strategy with surgical management reserved for selected patients.[2,8]

Patients with very short pain-free walking distance are typically candidates for revascularization. According to American College of Cardiologists/ American Heart Association (ACC/AHA) guidelines, endovascular treatment of SFA disease is indicated for individuals with significant disability due to intermittent claudication (IC) or CLI.

The femoropopliteal segment is a challenging vascular territory and has been among the least effective of all endovascular procedures in terms of long-term patency.[9,10,11] The SFA is the longest artery in the human body and is located between two major flexion points, the knee and the hip. The relatively small vessel lumen, in conjunction with a high plaque burden, slow flow, and a high frequency of primary occlusions, contributes to considerable technical difficulties. In recent years, however, improvements in device technology and the skill-sets of the interventionalists have facilitated the treatment of complex lesions, including long-segment chronic occlusions with or without moderate calcification. In fact, the current evolution towards treating more complex femoropopliteal lesions as seen in the renewed TransAtlantic Inter-Society Consensus (TASC) II recommendations clearly reflects the continuous evolutions in femoropopliteal stent design.[12] In most cases, the progression of atherosclerotic flow-limiting lesions in the blood vessels of the legs frequently involves the infra-popliteal arteries, resulting in a worsening diagnosis of CLI.

In the past, balloon angioplasty alone was the treatment of choice for the femoropopliteal artery segment. The TASC working group suggested that primary success rates were above 90% with a very low rate of complications (< 4%). However, within one year, patency failure rates above 70% were observed after balloon angioplasty in lesions longer than 10 cm.[13] The application of self-expanding nitinol stent technology seemed to improve the safety and durability of stenting in the SFA.[9,14,15,16] The theoretical basis for improved performance with the use of nitinol stents is due to the unique properties of nitinol such as flexibility, persistent radial force when oversized to a vessel, and ability for crush recovery in these high flexion and torsion force areas in the femoropopliteal arteries. In addition, self-expanding nitinol stents are

not as prone to external compression as are balloon-expandable stents. Moreover, due to its smaller arterial diameter and complex nature, the femoropopliteal segment does not respond well to rigid stents. As such, the most flexible nitinol stent is needed to mitigate stent fracture that often occurs in the femoropopliteal arteries.

Although above the knee use of nitinol Bare Metal Stents (BMS) is safe and feasible, it is evidently associated with significant neointimal hyperplasia and early restenosis,[17,18] which may be due to the chronic external forces on the vessel/stent interface resulting in a chronic stimulus for restenosis.[19] Therefore, the interest of investigators turned towards the pharmaceuticals such as paclitaxel and everolimus to suppress neointimal growth and restenosis after stent deployment. DES technology was developed to prevent early thrombosis and late luminal loss to potentially improve long-term patency rates for SFA.[20]

In a 2014 contemporary systematic review and meta-analysis, authors examined early outcomes of PTA, DESs, BMSs, or atherectomy for infrapopliteal atherosclerotic disease.[8] A total of 42 studies with 52 treatment arms representing 3,660 unique patients were included. Technical success rates were higher with bare metal stents (BMS; 98.6%) than with atherectomy (92.2%; P <.05) or Percutaneous Transluminal Angioplasty (PTA; 91.2%; P =.01), and higher with Drug-Eluting Stents (DES) than with PTA (P <.001). DES use had higher primary patency rates than atherectomy (P <.05), BMS use (P <.001), and PTA (P <.01). The 30-day rate of target lesion revascularization (TLR) was significantly higher with PTA (8.1%) than with BMS (2.2%; P <.05) and DES (1.1%; P <.05). Thirty-day rates of major unplanned amputation (range, 1.5%-4.4%) and mortality (range, 0.9%-3.3%) were comparable among treatment groups. Significant heterogeneity among studies was noted for most PTA outcomes. The authors concluded that early failure of percutaneous therapies in patients with infrapopliteal atherosclerotic lesions was both device- and technique-dependent. Specialty devices designed to reduce technical failure rates may therefore be of benefit in this selected group of patients.

Studies have shown that paclitaxel inhibits neointimal hyperplasia by disrupting normal microtubule function, thereby inhibiting smooth muscle cell migration, proliferation, and extracellular matrix secretion thus supporting short-term local delivery of paclitaxel for inhibiting restenosis in the SFA.[21,22]

6.2 ELUVIA Stent System

Boston Scientific Corporation (BSC) developed the ELUVIA stent, a paclitaxel-eluting, self-expanding nitinol stent, for use in the femoropopliteal arteries.

The ELUVIA Stent System leverages many successful BSC programs with global commercial approval for safe and efficacious use in subjects, and received CE-mark in February 2016. The ELUVIA stent and Stent Delivery System (SDS) is leveraged from the Innova™ Stent System, the drug coating polymers are leveraged from the PROMUS Element/PROMUS Element Plus Stent System, while the active pharmaceutical compound (paclitaxel) is leveraged from the TAXUS Element/ION Stent System.

6.3 MAJESTIC First Human Use Study

The MAJESTIC clinical study was the first BSC clinical study to evaluate a paclitaxel-eluting stent on a nitinol platform for use in SFA and/or PPA atherosclerotic lesions from 30 mm to 110 mm in length.

MAJESTIC is a prospective, single arm, multicenter clinical study. A total of 57 patients were enrolled at 14 centers in Europe, Australia, and New Zealand. Eligibility for the study included chronic lower limb ischemia defined as Rutherford categories 2, 3, or 4, and *de novo* or restenotic lesions (≥ 70% stenosis) located in the native superficial femoral artery or proximal popliteal artery with reference vessel diameter 4-6 mm and total lesion length ≥ 30 mm and ≤ 110 mm. The primary effectiveness endpoint was core laboratory-adjudicated 9-month primary patency (i.e., duplex ultrasound PSVR ≤ 2.5 and absence of TLR or bypass). Safety assessments included major adverse events defined as Clinical Events Committee (CEC)-adjudicated all-cause death through 1 month, target limb major amputation through 9 months, and TLR through 9 months.

Enrollment was completed in March 2014. Mean age (±SD) of the patients was 69.3±9.3 years and 83% were male; 35% had diabetes and 88% had a history of smoking. Rutherford category was 2 for 35%, 3 for 61%, and 4 for 4% of enrolled patients. Mean baseline lesion length was 70.8±28.1 mm and percent stenosis of the target lesions was 86.3%±16.2%. As presented at the 2015 Charing Cross Congress, the primary effectiveness endpoint of primary patency at nine months was 94.4%, with a one-sided lower 95% confidence bound of 86.3% that exceeded the performance goal of 75%. The nine-month composite MAE rate was 3.6%. The 3.6% MAE rate consisted of two TLR events through 9 months, with no all-cause death through 1 month, and no target limb major amputation through 9 months.

At 12 and 24 months, primary patency was 96.3% and 76.9% respectively. The composite rate of major adverse events (MAEs) through 12 months, 24 months and 36 months was 3.8%, 7.5% and 15.1% respectively. All MAEs that occurred in the study were TLRs. No stent fractures were identified.

In conclusion, the MAJESTIC results showed that patients whose femoropopliteal arteries were treated with the Eluvia stent sustained a high patency and low MAE rate through 36 months.

The MAJESTIC clinical investigation is complete.

6.4 IMPERIAL IDE Study

IMPERIAL is a global, prospective, multi-center trial evaluating the safety and effectiveness of the ELUVIA stent versus the Zilver PTX stent in the treatment of lesions 30-140 mm long located in the femoropopliteal arteries in subjects with symptoms classified as Rutherford categories 2-4. The trial consists of a prospective, multicenter, 2:1 randomized (ELUVIA vs Zilver PTX), controlled, single-blind, non-inferiority trial (RCT), a concurrent, non-blinded,

non-randomized, single-arm, pharmacokinetic (PK) substudy and a concurrent, non-blinded, non-randomized, single-arm Long Lesion substudy.

Up to 75 study centers worldwide enrolled subjects in the RCT. Regions participating include the United States, Canada, European Union, Japan and New Zealand. Approximately 10 study centers in the US enrolled subjects in the PK substudy. Any study center participating in the RCT could also enroll subjects in the Long Lesion substudy.

Enrollment was completed in February 2017. A total of 524 subjects were enrolled in the IMPERIAL trial: 465 subjects received treatment with either the investigational device (ELUVIA, N=310 subjects) or a control device (Zilver PTX, N=155 subjects) in the RCT, 13 subjects received treatment with the investigational device (ELUVIA) in the PK substudy and 50 subjects received treatment with the investigational device (ELUVIA) in the Long Lesion substudy.

Primary patency at 12 months was 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 was concluded to be non-inferior to Zilver PTX.

The MAE-free rate at 12 months was 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.

Also performed was a prespecified post-hoc superiority analysis of primary patency in the full-analysis cohort.

	Eluvia N=309 Subjects	Zilver PTX N=156 Subjects	Relative Risk [95% CI]	Difference [95% CI]	P-value
Patency at 12 Months					
Primary Patency[1]	86.8% (243/280)	77.5% (110/142)	1.12 [1.01, 1.24]	9.3% [1.4%, 17.3%]	0.0144

[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

In this head-to-head randomized trial, the primary non-inferiority endpoints for efficacy and safety at 12 months were met, and post-hoc analysis of the 12-month patency rate showed superiority for Eluvia over Zilver PTX.

The study is currently in long term follow up and is expected to be complete in 2022.

6.5 Summary

There is a large set of clinical data available for devices from which components have been leveraged for the ELUVIA Stent System. Successful results have been seen to date demonstrating safety and effectiveness for a variety of indications in coronary and peripheral

artery stenosis. The first results of the ELUVIA Stent System (MAJESTIC study) demonstrate a favorable effectiveness and safety profile.

Overall, the ELUVIA stent based on the Innova stent platform with additional paclitaxel coating is expected to reduce restenosis and improve long-term vascular patency and quality of life (QOL) compared to balloon angioplasty, balloon expandable stents, and nitinol BMS.

7. OBJECTIVES

The objective of the EMINENT Randomized Controlled Trial (RCT) is to confirm the superior effectiveness of the ELUVIA Drug-Eluting Vascular Stent System (ELUVIA Stent) for treating Superficial Femoral Artery (SFA) and/or Proximal Popliteal Artery (PPA) lesions up to 210 mm in length when compared against bare metal stents, and collect additional data including health economics data.

8. ENDPOINTS

The primary and secondary endpoints and additional endpoints will be evaluated on an intent-to-treat analysis and a per-treatment analysis. If a subject is randomized/enrolled but an ELUVIA stent or Self Expanding Bare Nitinol stent is not implanted, the subject will be followed through the 1 month follow-up visit only. Data to assess 1 month MAE rate will be collected for these subjects; other testing is not required.

8.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint assesses primary patency at 12 months post-procedure. This effectiveness endpoint is designed to demonstrate that the 12-month primary patency for the ELUVIA treatment group is superior to the Self-Expanding Bare Nitinol Stents treatment group.

Primary vessel patency is defined as a binary endpoint and will be determined to be a success when the duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) is ≤ 2.4 at the 12-month follow-up visit in the absence of clinically-driven TLR or bypass of the target lesion. All DUS readings will be assessed by an independent core laboratory.

Notes:

- Vessel patency is defined as freedom from more than 50% stenosis based on DUS PSVR comparing data within the treated segment to the proximal normal arterial segment.
- A PSVR >2.4 suggests >50% stenosis.
- The stented segment will be assessed for patency as a single segment regardless of the number of tandem lesions within the stented segment and regardless of the number of stents used to treat the tandem lesions.
- All DUS will be assessed by an independent core laboratory.

- Clinically-driven: A re-intervention within 5 mm proximal or distal to the original treatment segment for > 50% angiographic diameter stenosis in the presence of recurrent symptoms (≥ 1 change in Rutherford class) or associated with decreased ABI/TBI of ≥ 20% or ≥ 0.15 in the treated segment. Tibial Brachial Index (TBI) allowed in cases of incompressible vessels.

8.2 Secondary Endpoint

For the secondary endpoint Health-Economics data will be collected:

- Walking Improvement at 12 months assessed by change in Six Minute Hall Walk (6MHW) / treadmill test from baseline, or preceding any Target Vessel Revascularization
- Walking Improvement at 12 months assessed by change in Walking Impairment Questionnaire (WIQ) from baseline
- Quality of Life Improvement at 12 months assessed by change in EQ-5D-5L™ from baseline, or preceding any Target Vessel Revascularization
- Cost effectiveness of ELUVIA™ drug-eluting stent versus bare metal self-expanding nitinol stents
- Rate of Primary and Secondary Sustained Clinical Improvement at 12 months as assessed by changes in Rutherford Classification from baseline
- Rate of Hemodynamic Improvement at 12 months as assessed by changes in Ankle-Brachial Index (ABI) from baseline

8.3 Additional Endpoints

Additional endpoints that will be evaluated, but are not necessarily powered to make statistically based conclusions are as follows:

- Technical success defined as delivery and deployment of the assigned study stent to the target lesion to achieve residual angiographic stenosis no greater than 30% assessed visually
- Procedural success defined as technical success with no MAEs noted within 24 hours of the index procedure
- MAE rate (and individual components) at each time point, defined as all causes of death, target limb major amputation and/or TLR
- Survival rate at 4 years and 5 years post-procedure
- Primary Patency and Assisted Primary Patency at 6 months, 12 months, 24 months and 36 months using different DUS PSVRs
- Clinically-driven TLR and clinically-driven Target Vessel Revascularization (TVR) Rate at each time point
- Adverse Event Rates (unanticipated, major, serious, device/procedure-related) at each time point
- Number of Stent Fracture reported at 12 months and 24 months utilizing VIVA definitions

- Distribution of Rutherford Class during follow-up as compared to baseline at 1 month, 6 months, 12 months, 24 months and 36 months
- Walking Improvement at 1 month, 6 months, 24 months and 36 months assessed by change in Walking Impairment Questionnaire (WIQ) from baseline
- Quality of Life Improvement at 1 month, 6 months, 24 months and 36 months assessed by change in EQ-5D-5L™ from baseline
- Rate of Primary and Secondary Sustained Clinical Improvement as assessed by changes in Rutherford Classification from baseline at 1 month, 6 months, 24 months and 36 months
- Rate of Hemodynamic Improvement as assessed by changes in Ankle-Brachial Index (ABI) from baseline at 1 month, 6 months, 24 months and 36 months

9. STUDY DESIGN

The EMINENT Study is a prospective, multi-center, 2:1 randomized (ELUVIA vs Self-Expanding Bare Nitinol Stents), controlled, single-blind, clinical trial to confirm the effectiveness superiority and collect additional data including health economics data to support the use of the ELUVIA Drug-Eluting Vascular Stent System (ELUVIA Stent) versus Self-Expanding Bare Nitinol Stents in the treatment of lesions 30-210 mm long located in the femoropopliteal arteries in subjects with symptoms classified as Rutherford categories 2-4.

Both the test device and control devices are Nitinol stents and are CE-marked products commercially available in the regions included in this study. Both types of devices have already demonstrated their safety and effectiveness for treatment of SFA and/or PPA lesions.

The EMINENT Study is a single blind trial. Subjects will be blinded to treatment assigned and treatment received. All subjects must remain blinded until completion of all 12-month follow-up visits (primary endpoint). Packaging of the test and control devices are different, therefore the Investigator performing the procedure will not be blinded to the assigned treatment arm or resulting treatment. Study center personnel will be trained not to disclose the treatment assignment to the subject to minimize the potential unblinding of the subject. Site personnel conducting clinical follow-up assessments will be blinded to a subject's treatment assignment whenever possible, except when clinical follow-up visits are performed by the implanting Investigator. Duplex Ultrasound (DUS) Core Laboratory personnel, Angiography Core Laboratory personnel and the Clinical Events Committee (CEC) will be blinded to a subject's treatment assignment during the trial. Those involved in data analysis for the Sponsor will remain blinded until the primary endpoint analysis.

Instructions regarding the unblinding of a subject for a medical emergency can be found in the Unblinding Guidelines.

9.1 Scale and Duration

750 subjects will be enrolled in the EMINENT study to receive treatment with either the test device (ELUVIA, N=500 subjects) or a control device (Self-Expanding Bare Nitinol Stents, N=250 subjects).

The study will be conducted in up to 75 study centers in up to 15 European countries.

All subjects will be screened according to the protocol inclusion and exclusion criteria. Subjects meeting all inclusion criteria and no exclusion criteria will be randomized in a 2:1 allocation to either ELUVIA or Self-Expanding Bare Nitinol Stent. Randomization will be stratified to ensure equal distribution of ELUVIA and Self-Expanding Bare Nitinol Stents in lesions ≤110mm long and in lesions >110mm long.

Clinical follow-up will be required at the following time points: pre-discharge, 1 month (if standard of care), 6 months, 12 months, 24 months and 36 months post index procedure.

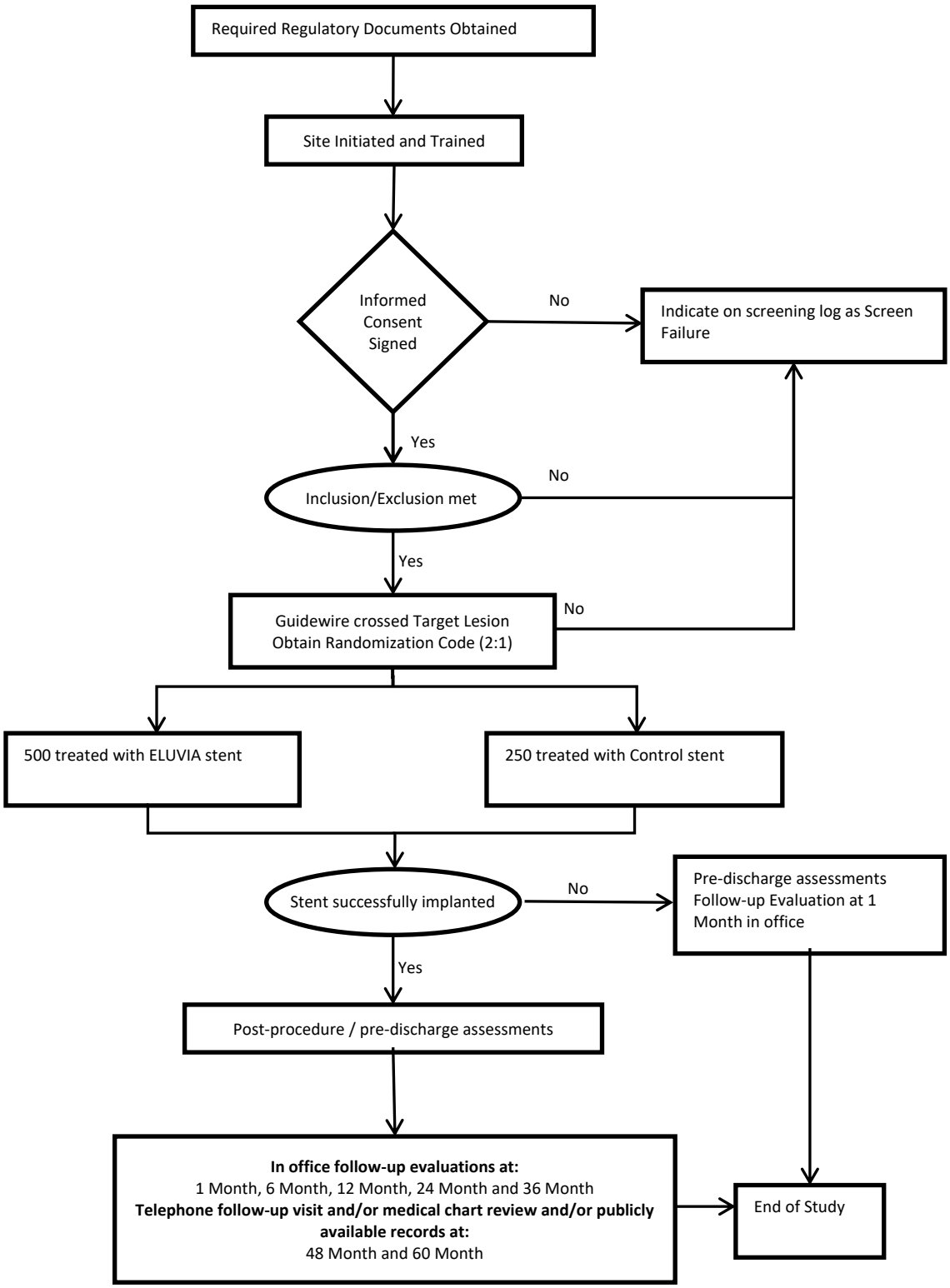
At 48 months and 60 months a telephone follow-up visit is required. If telephone visit is not completed, a medical chart review and/or publicly available records consultation will occur to verify survival status.

The enrollment period is expected to last approximately 18 months. No investigative site will be allowed to enroll more than 20 percent (150 subjects) of the total study population. The study will be considered complete (with regard to the primary endpoint) after all randomized/enrolled subjects have completed the 12 month follow-up visit, were discontinued prior to the 12 month follow-up visit, have died, or the last 12 month follow-up visit window is closed.

The study will be considered complete (with regard to all follow-up) after all randomized subjects have completed the 60 month (5 year) follow-up visit, were discontinued prior to the 60 month (5 year) follow-up visit, have died, or the last 60 month (5 year) follow-up visit window is closed.

It is estimated that it will take approximately 8 years to complete this study.

9.2 Study Flow Chart



10. STUDY POPULATION

10.1 Subject Selection

The intended population for this study are subjects who present with a lesion of 30-210 mm long located in the femoropopliteal arteries with symptoms classified as Rutherford categories 2-4.

Because selection of subjects, treatment of subjects, and evaluation of study data are potential sources of bias, methods are incorporated in the study design including (but not limited to):

- Subjects will be screened to confirm eligibility for enrollment with the pre-defined inclusion/exclusion criteria prior to enrollment.
- Demographics and medical history will be collected at baseline to allow assessment of characteristics that may influence study endpoints.
- Data collection requirements and study procedures will be standardized across all study sites.
- All investigational site personnel will be trained on and required to follow the Clinical Investigation Plan.
- Regular monitoring visits will be conducted to verify source data and adherence to the Clinical Investigation Plan and applicable regulations.
- An independent Clinical Events Committee (CEC) will be assigned to review and adjudicate the following endpoints and major adverse events reported by the trial Investigators: All Deaths, TLR, TVR, Target limb amputations, Stent Thrombosis.
- A Core Laboratory will be used to analyze angiography, DUS and X-ray images for the related endpoint evaluations.

To summarize, potential sources of bias that may be encountered in this clinical investigation have been considered and minimized by careful study design.

10.2 Inclusion Criteria

For inclusion in the study subjects must fulfil **ALL** of the following criteria:

1. Subjects age 18 and older
2. Subject is willing and able to provide consent before any study-specific test or procedure is performed, signs the consent form, and agrees to attend all required follow-up visits
3. Chronic, symptomatic lower limb ischemia defined as Rutherford categories 2, 3 or 4
4. Stenotic, restenotic or occlusive lesion(s) located in the native SFA and/or PPA:
    a. Degree of stenosis ≥70% by visual angiographic assessment
    b. Vessel diameter ≥ 4 and ≤6 mm

c. Total lesion length (or series of lesions) ≥ 30 mm and ≤210 mm (Note: Lesion segment(s) must be fully covered with one or two overlapping ELUVIA stent(s) or Self Expanding Bare Nitinol stent(s))
d. For occluded lesions (chronic occlusions) requiring use of re-entry device, lesion length ≤ 180 mm
e. Target lesion located at least three centimeters above the inferior edge of the femur

5. Patent infrapopliteal and popliteal artery, i.e., single vessel runoff or better with at least one of three vessels patent (<50% stenosis) to the ankle or foot with no planned intervention

10.3 Exclusion Criteria

Subjects are excluded if **ANY** of the following criteria are met:

1. Previously stented target lesion/vessel
2. Target lesion/vessel previously treated with drug-coated balloon <12 months prior to randomization/enrollment
3. Subjects who have undergone prior surgery of the SFA/PPA in the target limb to treat atherosclerotic disease
4. Use of atherectomy, laser or other debulking devices such as Rotarex in the target limb SFA/PPA during the index procedure
5. History of major amputation in the target limb
6. Documented life expectancy less than 24 months due to other medical co-morbid condition(s) that could limit the subject's ability to participate in the clinical study, limit the subject's compliance with the follow-up requirements, or impact the scientific integrity of the clinical study
7. Known hypersensitivity or contraindication to contrast dye that, in the opinion of the investigator, cannot be adequately pre-medicated
8. Known hypersensitivity/allergy to the test stent system or protocol related therapies (e.g., nitinol, paclitaxel, or structurally related compounds, polymer or individual components, and antiplatelet, anticoagulant, thrombolytic medications)
9. Platelet count <80,000 mm^3 or >600,000 mm^3 or history of bleeding diathesis
10. Concomitant renal failure with a serum creatinine >2.0 mg/dL
11. Receiving dialysis or immunosuppressant therapy
12. History of myocardial infarction (MI) or stroke/cerebrovascular accident (CVA) within 6 months prior to randomization/enrollment
13. Unstable angina pectoris at the time of randomization/enrollment
14. Pregnant, breast feeding, or plan to become pregnant in the next 5 years

15. Current participation in an investigational drug or device clinical study that has not completed the primary endpoint at the time of randomization/enrollment or that clinically interferes with the current study endpoints (Note: studies requiring extended follow-up for products that were investigational, but have become commercially available since then are not considered investigational studies)
16. Septicemia at the time of randomization/enrollment
17. Presence of other hemodynamically significant outflow lesions in the target limb requiring intervention at the time of the index procedure.
18. Presence of aneurysm in the target vessel
19. Acute ischemia and/or acute thrombosis of the SFA/PPA prior to randomization/ enrollment
20. Perforated vessel as evidenced by extravasation of contrast media prior to randomization/enrollment
21. Heavily calcified lesions
22. As applicable by French law, subject who is a protected individual such as an incompetent adult or incarcerated person

11. DEVICE DESCRIPTION

11.1 ELUVIA Drug-Eluting Stent System (Test Device)

The ELUVIA stent system is manufactured by Boston Scientific Corporation and comprised of the implantable endoprosthesis and the stent delivery system (SDS). The stent is a laser cut self-expanding stent composed of a nickel titantium 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 6 F 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. The delivery system is compatible with 0.035 in (0.89 mm) guidewires.

The ELUVIA stent system carries a drug/polymer coating formulation consisting of paclitaxel (the active ingredient), and PVDF-HFP Polymer Carrier (the inactive ingredient).

CE-mark for the ELUVIA stent system was obtained in February 2016.

11.1.1 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.

11.1.2 Primer Polymer and Drug Matrix Copolymer Carrier

The ELUVIA stent contains a primer polymer layer PBMA - poly (n-butylmethacrylate) between the bare metal stent and drug matrix layer. The drug matrix layer is comprised of a

semi-crystalline random copolymer, PVDF – HFP - poly(vinylidene fluoride-co-hexafluoropropylene), blended with paclitaxel.

11.1.3 ELUVIA Stent System Product Description

Characteristic	ELUVIA Stent System
Stent material	Nitinol
Drug product	Paclitaxel
Nominal Paclitaxel Content Range (based on stent length and diameter)	0.167µg/mm^2
Polymer(s)	Primer Layer: poly(n-butyl methacrylate) (PBMA) Active Layer: poly (vinylidene fluoride-co-hexafluoropropylene) (PVDF-HFP)
Delivery working length	75 cm, 130 cm
Stent delivery system (SDS)	6 F tri-axial system
Catheter shaft outer diameter	0.080 +/- 0.002”
Stent strut thickness	0.0039“strut width, 0.0086“ strut wall thickness

11.1.4 Test Device Sizes

The ELUVIA stent is available in a variety of diameters and lengths. The delivery system is offered in two working lengths (75 cm and 130 cm). The ELUVIA stent matrix included in the EMINENT Study is summarized in the below table.

SDS size	ELUVIA Stent sizes (mm)
75 cm	6.0 x 40, 6.0 x 60, 6.0 x 80, 6.0 x 100, 6.0 x 120, 6.0 x 150
130 cm	6.0 x 40, 6.0 x 60, 6.0 x 80, 6.0 x 100, 6.0 x 120, 6.0 x 150
75 cm	7.0 x 40, 7.0 x 60, 7.0 x 80, 7.0 x 100, 7.0 x 120, 7.0 x 150
130 cm	7.0 x 40, 7.0 x 60, 7.0 x 80, 7.0 x 100, 7.0 x 120, 7.0 x 150

11.2 Summary of Findings from Non-clinical Studies and Clinical Studies

A summary of all pre-clinical test results and the first clinical study performed with the ELUVIA stent system can be found in the Investigator’s Brochure (IB).

11.3 Device Accountability

Since both the test device and the control device are commercially available CE-marked devices, all devices used within the study will be used off-the-shelf. The Investigator must ensure that the device is used only in accordance with the Clinical Investigational Plan, IFU/DFU and IB.

The Principal Investigator or an authorized designee shall keep records documenting the use of test devices and control devices, which shall include the following for each identification of each device (lot number or unique code):

- Stent diameter and stent length
- Date of use
- Subject identification

Written procedures may be required by national regulations.

12. METHODS

The data collection schedule for the EMINENT study is summarized in section 4.

12.1 Screening

A Screening Log will be maintained by each investigational site to document selected information about subjects who have been screened for the study. For subjects who fail to meet the EMINENT trial eligibility criteria, including the reason for screen failure.

12.2 Informed Consent

Prior to any study-related procedure a signed informed consent form has to be obtained from every subject.

The investigator or responsible medical staff (as allowed per national law) will explain the nature, purpose and risks of the study and provide the subject with a copy of the patient information sheet.

The person obtaining consent will avoid any coercion or undue improper influence on or inducement of the subject to participate. They will not waive or appear to waive the subject's legal rights. They will use native non- technical language that is understandable to the subject. The refusal of a subject to participate in the study or a subject's decision to withdraw from the study must never interfere with the patient-doctor relationship.

The subject will be given sufficient time to consider the implications of study participation before making a decision.

Study personnel should explain to the subject that even if the subject agrees to participate in the trial and signs the ICF, catheterization may demonstrate that the subject is not a suitable candidate for the trial.

Should there be any amendments to the Clinical Investigational Plan, which would directly affect the subjects' participation in the study, e.g. a change in any procedure, the informed consent form must be amended to incorporate this modification and all subjects must agree to sign this amended informed consent form to confirm that they re-consent to continue their participation in the study.

The original signed copy of the patient's informed consent form must be maintained in the study files. The subject should receive a copy of the signed informed consent form. The consent process and subject's study participation should be indicated in the patient's medical records.

12.3 Point of Enrolment

Once the subject has signed the Informed Consent Form, and has met all clinical inclusion and no clinical exclusion criteria, the subject will be considered eligible to be enrolled in the trial. If the subject is found to meet exclusion criteria during the angiographic eligibility assessment, the subject will be considered a screen failure and should not be enrolled/randomized, nor should the subject be followed post-procedure per protocol.

If the subject is found to meet the eligibility criteria during the angiographic phase of the procedure, the subject will be considered eligible to be randomized/enrolled. After the Investigator successfully crosses the target lesion with the guidewire, the subject will be randomized using the eCapture EDC database to either the test device group or the control device group. Subjects will be considered enrolled in the study after they have been successfully randomized (i.e. when a treatment assignment is received by the study site).

12.4 Study Assessments and Endpoint Measurements

12.4.1 Pre-Procedure Assessments – Up to 30 Days

The following pre-procedure data must be collected within 30 days prior to the index procedure (unless otherwise specified) for all subjects:

- Demographics and medical history
- Physical assessment including:
    - Rutherford Category Assessment
    - Ankle-Brachial Indices (ABI) measurements
- Laboratory tests
    - Serum creatinine
    - Platelet Counts
- Confirmation that all clinical inclusion/exclusion eligibility criteria have been met
- 6-Minute Hall Walk or treadmill test (whatever is standard of care)
- Administer Questionnaire Assessments
    - Walking Impairment Questionnaire (WIQ)
    - EQ-5D-5L

12.4.2 Pre-Procedure Assessments – Up to 7 Days

The following pre-procedure data must be collected within 7 days prior to the index procedure (unless otherwise specified) for all subjects:

- Pregnancy test for females of childbearing potential with analysis per local practice (serum and/or urine)
- Antiplatelet medication usage (if applicable)

12.4.3 Procedure

Investigators will manage the cardiovascular risk factors and comorbidities for all subjects according to standard care. Investigators should ensure close monitoring of the amount of contrast for subjects with elevated serum creatinine levels and consider preventive measures (medication and hydration) to reduce the risk of contrast-induced nephropathy (CIN).

Diagnostic angiography of the lower extremities must be performed using standard techniques to confirm angiographic eligibility of the target lesion. Visual angiographic assessment may be used to determine if criteria are met.

Angiographic images must be sent to the Angiographic Core Laboratory for evaluation.

A Treatment of iliac lesions

Using the same access site, Iliac lesion(s) in both limbs may be treated during the index procedure.

Iliac lesions in the target limb should be treated ***prior to*** the target SFA/PPA lesion with commercially available devices (non-drug-eluting in the target limb) and treatment must be considered successful (i.e. residual stenosis <30% and no clinical events [embolization, perforation])

If the above criteria are not met, the subject may not be randomized, but may be rescreened for eligibility after 30 days.

Besides the target lesion, only iliac lesions can be treated during the index procedure. If nonTarget, nonIliac lesions in either limb are to be treated they must be treated in a separate procedure either before or after the index procedure.

B Randomization

The start of the index procedure is defined as the time of guide catheter insertion into the sheath for the target limb SFA/PPA interventional procedure.

During catheterization, the following procedures and assessments must be completed for the Target Lesion.

- Perform angiography according to the Core Lab guidelines.
- Confirm angiographic eligibility criteria of the target lesion or tandem lesion(s).
- Cross target lesion using guidewire or re-entry device.

- After target lesion is crossed by the guidewire, access the randomization custom function in eCapture EDC to randomize subject.
- If randomized to ELUVIA, retrieve an appropriately sized test stent from commercial inventory to adequately cover the target lesion with one or two stents, if necessary.
- If randomized to the control group, retrieve an appropriately sized control stent from commercial inventory of the per-protocol allowed self-expanding stents - Bare Nitinol (Supera, Lifestent, Everflex, S.M.A.R.T. Flex, S.M.A.R.T. Control, Pulsar, COMPLETE SE, Misago or Innova) to adequately cover the target lesion with one or two stents, if necessary.

Note: If difficulties are encountered when accessing the randomization custom function in the eCapture EDC system, the subject should not be enrolled in the trial.

Note: Bypassing the randomization process and manually assigning treatment type is not allowed.

C Target Lesion Stent Placement

The target lesion is a lesion selected by the Investigator for treatment with either the test or control device. The target lesion must meet all angiographic selection criteria. The target lesion may include two or more tandem lesions, provided that the entire segment of tandem lesions is ≤210 mm and can be covered with one single stent or two overlapping stents (ELUVIA or Control stent) according to each device's IFU/DFU. For occluded lesions (chronic occlusions) requiring the use of a re-entry device, the target lesion length must be ≤ 180 mm allowing the target lesion and re-entry area to be covered with one or two stent(s) (ELUVIA or Control stent) (Refer to Inclusion criterion 4c and 4d).

Procedural information must be reported (specific data fields are noted in the electronic database). Refer to the IFU/DFU for detailed instructions about delivery system preparation and placement of the ELUVIA stent or the Control stent.

Procedural recommendations:

Use of a radiopaque ruler or other standard is recommended to help with calibration.

Optimal target lesion/vessel preparation is recommended.

Pre-dilation of the target lesion with optimally sized balloon(s) (nominal size of artery) is recommended before stent placement, but is at the discretion of the implanting Investigator. After stent placement, the Investigator should ensure that the stent is in full contact with the arterial wall. In order to achieve full contact, post-dilatation may be performed at the discretion of the Investigator. Drug coated balloons cannot be used for pre- or post-dilating the target vessel. Peri-stent dissections should be treated conservatively, with low pressure prolonged balloon inflation, or with additional study stent implantation per standard practice. Haziness, lucency, or filling defects within or adjacent to the stent, and angiographic complications such as distal thromboemboli or no reflow, should also be treated per standard

practice. All angiographic complications that occur should be documented by angiography and submitted to the Angiographic Core Laboratory for analysis.

ELUVIA

Prior to use of the test device, the treating physician must carefully read and be familiar with the entire DFU. The ELUVIA DFU must be followed for implanting the test stent. Anticoagulant therapy should be consistent with guideline practices and the hospital standard of practice during the procedure.

Control Self-Expandable Bare Nitinol Stent

Prior to use of the control device, the treating physician must carefully read and be familiar with the entire IFU packaged with the commercial stent. Anticoagulant therapy should be consistent with guideline practices and the hospital standard of practice during the procedure.

NOTE: If an additional stent is required due to complications (e.g., dissection, misplacement or under-sizing of the target lesion), the additional stent placed should be a stent of the same type used to treat the target lesion.

D Post-procedure Angiogram

Perform the post-procedure angiography according to the Angiographic Core Laboratory procedure guidelines. The final angiogram must be performed and recorded, including distal run-off. Angiographic images must be sent to the angiographic core laboratory for evaluation.

E End of the Index Procedure

The end of the index procedure is defined as the time the guide (catheter or sheath) is removed (post final angiography). The introducer(s) sheaths should be removed as per standard local practice. The following procedures must be completed:

- Document procedural, target lesion, pre-dilatation, post-dilatation (if applicable), and study stent information on the appropriate eCRFs
- Record antithrombotic medications
- Complete AE assessment (SADEs, UADEs and ADEs/Device Deficiencies)
- Finalize angiographic procedure film and related required documentation to submit to the Core Laboratory per instructions set in the Core Lab Guidelines.

12.5 Post-procedure/Pre-hospital Discharge

The subject may be discharged from the hospital when clinically stable at the Investigator's discretion. The following assessments must be completed prior to hospital discharge.

- Medication assessment
- AE assessment (SADEs, UADEs and ADEs/Device Deficiencies)
- Health care costs associated with index procedure

It is important that trial site personnel review the trial requirements with the subject to maximize compliance with the follow-up schedule and required medication regimen. It is also

important that trial site personnel instruct subjects to return for follow-up assessments according to the trial event schedule. Study staff should establish a date for the follow-up visit with the subject and if possible, schedule the visit at the time of hospital discharge.

Note: Subjects will be blinded to treatment assigned and treatment received. All subjects must remain blinded until completion of all 12-month follow-up visits (primary endpoint).

12.6 Angiography

All subjects will undergo angiographic assessment during the index procedure per standard of care. Subjects requiring reintervention of the target vessel during the 36 month follow-up period will undergo angiographic assessment at the time of reintervention as standard of care.

Angiographic data and images collected during the index procedure and during any reinterventions of the target vessel during the 36 month follow-up period must be forwarded to the Angiographic Core Laboratory for analysis. Angiograms performed at outside institutions should also be sent to the Core Laboratory. Angiograms will be centrally assessed by the Angiographic Core Laboratory, for qualitative and quantitative analysis.

12.7 Visit Windows

Table 12.7-1: Protocol Visit Windows

Visit	Visit windows
Informed consent	Prior to any trial procedures
Pre-procedure	Testing ≤ 30 days prior to procedure unless otherwise specified
Index Procedure	Time point = zero
1 month post procedure	30 days (-7/+14 days) from procedure date
6 months post procedure	182 days (+/- 30 days) from procedure date
12 months post procedure	365 days (+/- 30 days) from procedure date
24 months post procedure	730 days (+/- 30 days) from procedure date
36 months post procedure	1095 days (+/- 30 days) from procedure date

Table 12.7-2: Telephone/medical chart/public record Follow-up Windows

Telephone call/Medical chart/public record	Target Date
48-Months	1460 days (+/- 90 days) from procedure date
60-Months	1825 days (- 90/+30 days) from procedure date

12.8 Follow-up Visits

EMINENT is a single blind trial. Site personnel conducting clinical follow-up will be blinded to a subject's treatment assignment whenever possible.

All randomized/enrolled subjects who receive a test or control stent, will be evaluated prior to discharge from the index procedure and at 1 month (if local standard of care), 6 months, 12 months, 24 months, 36 months, 48 months, and 60 months after the index procedure.

Subjects who underwent advancement of the test or control stent system into the body but a stent was not implanted will be considered enrolled and will be followed for safety through the 1-month follow-up visit only. Data for assessment of MAE will be collected for these subjects; other testing is not required.

For each follow-up visit, the results of the subjects' clinical status and functional testing (Rutherford Categorization and ABI) should be completed prior to initiating the DUS imaging, if required. Subjects requiring re-intervention should be treated according to the Investigator's discretion and standard of care. These subjects should receive an approved, commercially available treatment (if appropriate).

Note: Follow-up ultrasounds will not be required for any subject who underwent bypass surgery of the target lesion during the 60 month follow-up timeframe, or has a documented occluded stent.

Note: In case a subject undergoes a re-intervention of the target vessel, it is recommended to perform a walking test (6MWT or treadmill test) and QoL questionnaire (EQ-5D-5L™) prior to the Target Vessel Revascularization.

As documented in section 12.10, a minimum of 3 attempts (i.e., 2 phone calls followed by a certified letter, or other traceable letter) shall be made to contact the subject or subject's next of kin to complete the follow-up visits.

If a visit is not completed, contact attempts will be documented in the medical chart and a medical chart review and/or publicly available records review will occur to asses and report survival status.

Requirements of each follow-up evaluation are described below.

12.8.1 1-Month Follow-up Visit

Subjects will be evaluated 1 month after the index procedure, if the 1 month visit is local standard of care. The following assessments must be performed during the 1 Month office visit. For enrolled subjects who did not have a stent implanted, the AE assessment is required; no other tests are required. Site personnel conducting clinical follow-up will be blinded to a subject's treatment assignment whenever possible.

- Rutherford Categorization
- ABI Measurements *(may be collected immediately post-procedure through 1 Month Follow-up window [Day 0 – 44])*
- Walking Impairment Questionnaire
- EQ-5D-5L Questionnaire
- Healthcare utilization information (including health care costs collected via standardized form)
- Adverse Events Assessment (protocol defined Major Adverse Events, SADEs, UADEs and ADEs/Device Deficiencies)
- Medication Assessment

12.8.2 6-Month Follow-up Visit

All enrolled subjects must be evaluated 6 months after the index procedure. The following assessments must be performed during the 6 Month office visit. Site personnel conducting clinical follow-up will be blinded to a subject's treatment assignment whenever possible.

- Rutherford Categorization
- ABI Measurements
- Walking Impairment Questionnaire
- EQ-5D-5L Questionnaire
- DUS of stented segment performed according to the Core Lab guidelines
- Healthcare utilization information (including health care costs collected via standardized form)
- Adverse Events Assessment (protocol defined Major Adverse Events, SADEs, UADEs and ADEs/Device Deficiencies)
- Medication Assessment

12.8.3 12-Month Follow-up Visit

All enrolled subjects must be evaluated 12 months after the index procedure. The following assessments must be performed during the 12 Month office visit. Site personnel conducting clinical follow-up will be blinded to a subject's treatment assignment whenever possible.

- Rutherford Categorization
- ABI Measurements
- 6-Minute Hall Walk or treadmill test (whatever is standard of care)
- Walking Impairment Questionnaire
- EQ-5D-5L Questionnaire
- DUS of stented segment performed according to the Core Lab guidelines
- X-ray of the stented segment (only if performed per standard of care)
- Healthcare utilization information (including health care costs collected via standardized form)
- Adverse Events Assessment (protocol defined Major Adverse Events, SADEs, UADEs and ADEs/Device Deficiencies)
- Medication Assessment

Subjects and site personnel conducting clinical follow-up may be unblinded after completion of this visit, following confirmation from the Sponsor (after completion of all 12-month follow-up visits).

12.8.4 24-Month Follow-up Visit

All enrolled subjects must be evaluated 24 months after the index procedure. The following assessments must be performed during the 24 Month office visit.

- Rutherford Categorization
- ABI Measurements
- Walking Impairment Questionnaire
- EQ-5D-5L Questionnaire
- DUS of stented segment performed according to the Core Lab guidelines

- X-ray of the stented segment (only if performed per standard of care)
- Healthcare utilization information (including health care costs collected via standardized form)
- Adverse Events Assessment (protocol defined Major Adverse Events, SADEs, UADEs and ADEs/Device Deficiencies)
- Medication Assessment

12.8.5 36-Month Follow-up Visit

All enrolled subjects must be evaluated 36 months after the index procedure. The following assessments must be performed during the 36 Month office visit.

- Rutherford Categorization
- ABI Measurements
- Walking Impairment Questionnaire
- EQ-5D-5L Questionnaire
- DUS of stented segment performed according to the Core Lab guidelines
- Healthcare utilization information (including health care costs collected via standardized form)
- Adverse Events Assessment (protocol defined Major Adverse Events, SADEs, UADEs and ADEs/Device Deficiencies)
- Medication Assessment

12.8.6 48- and 60-Month Follow-up Visits

At 48 months and 60 months post procedure, a telephone follow-up visit will occur with the subject. If a telephone visit is not completed, a medical chart review and/or publicly available records review will be conducted to asses and report survival status.

Data Collection Requirements for the 48- and 60-months telephone/medical chart review/ publicly available records follow-ups:

- Adverse Events Assessment (protocol defined Major Adverse Events, SADEs, UADEs and ADEs/Device Deficiencies)
- Survival status

As documented in section 12.10, a minimum of 3 attempts (i.e., 2 phone calls followed by a certified letter, or other traceable letter, if necessary) shall be made to contact the subject or subject's next of kin to complete the 48- and 60-Month telephone visits. Contact attempts will be documented in the medical chart.

12.9 Trial Completion

The trial will be considered complete (with regard to the primary endpoints) after all subjects have completed the 12-month follow-up visit, were discontinued prior to the 12-month follow-up visit, have died or the follow-up visit window is closed.

The trial will be considered complete (with regard to all follow-up) after all subjects have completed the 60 month (5 year) follow-up visit, were discontinued prior to the 60 month (5 year) follow-up visit, have died or the follow-up visit window is closed.

12.10 Missed or Late Visits

Every effort must be made by the site to retain study subjects for the duration of the study.

A minimum of 3 attempts (i.e., 2 phone calls followed by a certified letter, or other traceable letter, if necessary) should be made to contact the subject or subject's next of kin for each missed follow-up visit and this information should be documented in the source. Missed or late visits will be recorded as Protocol Deviations.

No subject will be considered lost to follow-up prior to the 12 Month follow-up visit in order to make every effort to collect evaluable data for the primary endpoint. A subject will be considered lost to follow-up after the subject:

1. misses 2 consecutive annual follow-up visits without due cause **and**
2. medical chart review/public records consultation are inconclusive as to subject's survival status.

12.11 Medication

Investigators must prescribe concomitant anti-coagulant and anti-platelet medications consistent with current local clinical practice. Antiplatelet medication usage will be collected and reported in the electronic case report form (eCRF) from the time of the pre-procedure visit through the 36 month (3 year) follow-up visit. Additional concomitant medications may be prescribed at the discretion of the treating physician according to standard of care.

12.12 Withdrawal of Individual Subjects

Subjects may leave the study at any time for any reason and without any consequences. The investigator or designee will try to obtain the reason for study withdrawal and document this in the source data.

If a subject chooses to withdraw from the study, no further study-specific evaluation(s) should be performed, and no additional data will be collected. The sponsor may retain and continue to use any data collected prior to the withdrawal of consent, unless specified differently by the subject. The subject will return to the care of their personal physician.

Subjects voluntarily withdrawing from the trial will be asked to participate in a limited capacity allowing their medical status to be followed by telephone contact, medical chart review, or by other agreed upon method.

If a subject decides not to continue participation in a limited capacity, the investigator will not access their medical record or other confidential records for new purposes related to the study; however, study data collected prior to their withdrawal may be reviewed and publicly available records may be consulted prior to or after their withdrawal. Note: this applies to all withdrawn subjects (e.g., withdrawn by investigator).

If a subject is withdrawn from the study, the investigator will promptly inform the subject and sponsor. Withdrawn subjects will be followed according to the investigational center's standard procedures. Serious adverse device-effects that are still ongoing at the end of the subject's participation in the trial will be followed up for resolution status.

12.13 Replacement of Individual Subjects after Withdrawal

Subjects who exit the study prematurely will not be replaced.

13. SUSPENSION OR TERMINATION

13.1 Premature Termination of the Study

Early termination of the study is the closure of the clinical study that occurs prior to meeting defined endpoints. Early termination is possible for the whole study or a single site. Study suspension is a temporary postponement of study activities related to enrollment. Suspension is possible for the whole study or a single site.

13.1.1 Study-wide Termination or Suspension

The sponsor reserves the right to terminate the study at any stage but intends to exercise this right only for valid scientific or administrative reasons and reasons related to protection of subjects. Investigators, associated Ethics Committees (ECs), and regulatory authorities, as applicable, will be notified in writing in the event of study termination. Possible reasons for premature study termination include, but are not limited to:

- The occurrence of unanticipated adverse device effects that present a significant or unreasonable risk to subjects enrolled in the study
- An enrollment rate far below expectation that prejudices the conclusion of the study
- A decision on the part of the sponsor to suspend or discontinue development of the device

13.1.2 Investigator/Site Termination or Suspension

Possible reasons for clinical investigator or site termination or suspension include but are not limited to:

- Failure to obtain initial Ethics Committee approval or annual renewal of the study, if applicable
- Persistent non-compliance to the Clinical Investigation Plan (e.g. failure to adhere to inclusion/exclusion criteria, failure to follow subjects per scheduled follow-ups)
- Lack of or insufficient enrollment
- Noncompliance to regulations and/or the terms of the Clinical Trial Agreement (e.g. failure to submit data in a timely manner, failure to follow up on data queries and monitoring findings in a timely manner, etc.)
- Ethics Committee suspension of the site
- Fraud or fraudulent misconduct is discovered
- Investigator request (e.g. no longer able to support the study)

13.1.3 Procedures for Termination or Suspension

A Sponsor-initiated and regulatory authority-initiated

- Sponsor will promptly inform the clinical investigators of the termination or suspension and the reasons and inform the Regulatory Authority(ies) where required.
- In the case of study termination or suspension for reasons other than a temporary Ethics Committee approval lapse, the investigator will promptly inform the Ethics Committee.
- In the case of study termination, the investigator must inform the Subjects and may inform the personal physician (if allowed) of the subjects to ensure appropriate care and follow-up is provided.
- In the case of a study suspension, subject enrollment must stop until the suspension is lifted by sponsor and approved by the applicable committees/authorities.
- In the case of a study suspension, enrolled subjects should continue to be followed out of consideration of their safety, rights and welfare.

B Investigator-initiated

- The investigator will inform sponsor and provide a detailed written explanation of the termination or suspension.
- The investigator will promptly inform the institution (where required per regulatory requirements).
- The investigator will promptly inform the Ethics Committee and sponsor will promptly inform the Regulatory Authority (where applicable).
- The investigator will promptly inform the subjects and/or the personal physician of the subjects to ensure appropriate care and follow-up is provided.
- In the case of a study suspension, subjects enrolled should continue to be followed out of consideration of their safety, rights and welfare.

C Ethics Committee or Regulatory Authority-initiated

- The investigator will inform sponsor and provide a detailed written explanation of the termination or suspension within 5 business days.
- Subject enrollment must stop until the suspension is lifted.
- Subjects already enrolled should continue to be followed in accordance with Ethics Committee/ Regulatory Authority policy or its determination that an overriding safety concern or ethical issue is involved.

14. SAFETY

It is the responsibility of the investigator to assess and report to sponsor any event experienced by the study subject after randomization/enrollment, whether during or subsequent to the procedure, and which falls under any of following categories:

- All Device and/or Procedure Related (Serious) Adverse Events
- All Device Deficiencies

- Unanticipated Adverse Device Effects/Unanticipated Serious Adverse Device Effects
- All Events which meet the per-protocol definition of Major Adverse Event (note: for target limb amputations, both minor and major amputations should be reported)
- All Target Vessel Revascularizations (TVR)
- New findings/updates in relation to already reported events

When possible, the medical diagnosis should be reported as the Event Term instead of individual symptoms.

If it is unclear whether or not an event fits one of the above categories, or if the event cannot be isolated from the device or procedure, it should be submitted as an adverse event and/or device deficiency.

Underlying diseases are not reported as AEs unless there is an increase in severity or frequency during the course of the trial.

Death should not be recorded as an AE, but should only be reflected as an outcome of a specific SAE (see below for AE definitions).

Refer to Section 15 for the known risks associated with the study device(s).

Device deficiencies and other device issues should not be reported as AEs. Instead, they should be reported on the appropriate eCRF per the study CRF Completion Guidelines. If an AE results from a device deficiency or other device issue, the AE should be reported on the appropriate eCRF.

14.1 Adverse Events

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device.

NOTE 1: This definition includes events related to the test device or the comparator
NOTE 2: This definition includes events related to the procedures involved.
NOTE 3: For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse events will be monitored throughout the study. Investigators must obtain all information available to determine the causality and outcome of the AE and to assess whether it meets the criteria for classification as a serious adverse device effect requiring immediate notification to the sponsor or its designated representative. All reported ADEs will be documented on the appropriate CRF and will include the event description [diagnosis – only signs or symptoms in case underlying diagnosis is not (yet) known], onset, resolution, seriousness, severity, cause and action taken. The investigator must assess causality and severity for all ADEs.

All ADEs will be followed by the Investigator until resolution or until the end of study participation.

14.2 Adverse Device Effects

An adverse device effect (ADE) is an AE related to the use of a medical device.

NOTE 1: This definition includes adverse events resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the medical device.

NOTE 2: This definition also includes any event that is a result of a use error or intentional abnormal use of the medical device.

14.3 Serious Adverse Events

An adverse event is defined as serious (SAE), whenever the adverse event

a) led to death,
b) led to serious deterioration in the health of the subject, that either resulted in
   1) a life-threatening illness or injury, or
   2) a permanent impairment of a body structure or a body function, or
   3) in-patient hospitalization or prolongation of existing hospitalization, or
   4) medical or surgical intervention to prevent life-threatening illness, or
   5) injury or permanent impairment to a body structure or a body function,
c) led to fetal distress, fetal death or a congenital abnormality or birth defect

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the Clinical Investigational Plan, without a serious deterioration in health, is not considered a serious adverse event.

14.4 Serious Adverse Device Effects

A serious adverse device effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

14.5 Unanticipated Serious Adverse Device Effects

An unanticipated serious adverse device effect (USADE) is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

NOTE: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk analysis report.

14.6 Device Malfunction/Failure/Deficiency – Device Specific Events

Device deficiency is the inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

NOTE: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer.

Device malfunction means the failure of a medical device to perform in accordance with its intended purpose when used in accordance with the IFU/DFU, IB or Clinical Investigational Plan.

Device Deficiencies (DD) and other device issues should not be reported as AEs. Instead, they should be reported on the appropriate eCRF per the study CRF Completion Guidelines. If an AE results from a device deficiency or other device issue, the AE should be reported on the appropriate eCRF.

Device malfunction/failures/deficiencies may or may not result in the subject experiencing harmful effect. All AEs/SAEs associated with a device failure are by definition device-related.

14.7 Adverse and serious adverse events reporting

Timely, accurate, and complete reporting and analysis of safety information for clinical studies are crucial for the protection of subjects. Reporting and analysis of safety data are mandated by regulatory authorities worldwide. Since the safety reporting requirements and classification systems vary for each Regulatory Authority, requirements from all geographies are taken into account for the collection and reporting of safety information.
Subjects will be carefully monitored during the study for possible adverse events. Any adverse event that occurs after the time of randomization/enrollment through end of study participation will be fully evaluated by the Investigator. Appropriate treatment will be initiated and the study follow up will continue as completely as possible.

The Investigator will document all observations and clinical findings of adverse events, including the nature, severity and relationship, on the appropriate CRFs.

The Investigator is required to report all SADEs to the Sponsor within 3 calendar days of awareness of the event. UADEs/USADEs need to be reported to the Sponsor within 1 business day of awareness of the event. Initial reporting may be done by phone, fax, email or by completing the applicable CRF form with as much information as available at that time. In case of urgent questions regarding safety reporting, please contact the study contact as indicated in your study contact list.

Additionally, device deficiencies should be reported to the Sponsor within 3 calendar days of awareness.

ADEs should be reported in a timely manner (recommended within 10 business days) of awareness.

Furthermore, the Investigator must follow their local Ethics Committee policy for SADE/UADE/USADE reporting. If required by national regulations or Ethics Committee, device deficiencies that could have led to a SADE should be reported to the Sponsor or designee and Ethics Committee within 3 calendar days of awareness of the event.
As additional information becomes available, the Investigator will record all adverse device effects (anticipated and unanticipated) and device deficiencies on the appropriate CRFs.

In case of Major Adverse Events, copies of source documentation which contain significant information related to the event such as discharge letters, surgery reports, consultation letters, ECGs, laboratory results, etc. are required for evaluation of the event. Copies of such documentation shall be obtained from the investigator, blinded / de-identified as to the subjects' identity, and provided to the Sponsor or designee.

Regarding subject deaths, it is requested that a copy of the death certificate and a copy of the autopsy report (if applicable), be sent to the sponsor or designee when available. Any other source documents related to the death should also be provided to the sponsor or designee. In the event that no source documents are available, the PI is required to describe the circumstances of the subject's death in a letter, e-mail or other written communication.

UADEs/USADEs have special reporting requirements. The Sponsor will notify the sites, ECs and regulatory bodies as per country specific regulations.

14.8 Annual Safety Report

In addition to the expedited reporting of SADEs, the sponsor will submit, at a minimum once a year throughout the clinical study, an annual safety report to the involved ethical committees and competent authorities of the concerned Member States if required. This annual safety report can be combined with the annual progress report.

14.9 Severity

The investigator will use the following definitions to determine the severity of an adverse event:

- ***Mild:*** Awareness of a sign or symptom that does not interfere with the subject's usual activity or is transient, resolved without treatment and with no sequelae.
- ***Moderate:*** *Interferes with the subject's usual activity and/or requires symptomatic treatment.*
- ***Severe:*** *Symptom(s) causing severe discomfort and significant impact of the subject's usual activity and requires treatment. Relationship to the device or procedure*

The investigator will use the following definitions to assess the relationship to the device or procedure:

Not Related:

Relationship to the device or procedure can be excluded when:

- the event is not a known side effect of the product category the device belongs to or of similar devices and procedures;
- the event has no temporal relationship with the use of the device or the procedure;
- the event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
- the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the event;
- the event involves a body-site or an organ not expected to be affected by the device or procedure; the event can be attributed to another cause (e.g. an

underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);

- the event does not depend on a false result given by the device used for diagnosis, when applicable; harms to the subject are not clearly due to use error;
- In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.

Unlikely Related:

The relationship with the use of the device or procedure seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.

Possibly Related:

The relationship with the use of the device or procedure is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible related.

Probably Related:

The relationship with the use of the device or procedure seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.

Causal Relationship:

The event is associated with the device or with procedure beyond reasonable doubt when:

- the event is a known side effect of the product category the device belongs to or of similar devices and procedures;
- the event has a temporal relationship with device use/application or procedure;
- the event involves a body-site or organ that
    - the device or procedure are applied to;
    - the device or procedure have an effect on;
- the event follows a known response pattern to the medical device (if the response pattern is previously known);
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible);
- other possible causes (e.g. an underlying or concurrent illness/clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
- harm to the subject is due to error in use;

- the event depends on a false result given by the device used for diagnosis, when applicable;
- In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedure and the event

If the relationship between any adverse event and the use of the device is considered to be unlikely, possibly or probably related, that event will be classified as an ADE or SADE.

14.10 Clinical Events Committee (CEC)

The CEC is an independent group of individuals with no affiliation with BSC. Committee membership will include practitioners of peripheral endovascular procedures, as well as other experts with the necessary therapeutic and subject matter expertise to review and adjudicate the following endpoints and major adverse events reported by the trial Investigators:

- All Deaths
- Target Lesion Revascularizations
- Target Vessel Revascularizations
- Target limb amputations
- Stent Thrombosis

CEC members will be blinded to a subject's treatment assignment during the trial.

Responsibilities, qualifications, membership, and committee procedures are outlined in the CEC charter.

15. POTENTIAL RISKS AND BENEFITS

15.1 Anticipated Adverse Events and Risks Associated with Use of the ELUVIA Stent System and Implantation of the ELUVIA Stent

The risks associated with the implantation of a stent in the SFA/PPA may include, but are not limited to the following:

- Allergic reaction (to drug/polymer, contrast, device or other)
- Bleeding/Hemorrhage
- Death
- Embolization (air, plaque, thrombus, device, tissue or other)
- Extremity ischemia/amputation
- Hematoma
- Need for urgent intervention or surgery
- Pseudoaneurysm formation
- Renal insufficiency or failure
- Restenosis of stented artery

- Sepsis/infection
- Thrombosis / thrombus
- Tissue ischemia / necrosis
- Transient hemodynamic instability (hypotensive/hypertensive episodes)
- Vasospasm
- Vessel injury, including perforation, trauma, rupture and dissection
- Vessel occlusion

15.2 Risks Associated with the Test Device Unique to Paclitaxel drug coating

Certain side effects and discomforts have been reported in subjects that have received paclitaxel in intravenous forms as part of chemotherapy treatment. These subjects may have other comorbid conditions and/or have received concomitant medications that may also contribute to the reported side effects. Under these circumstances the dose is delivered throughout the body by the blood and in doses hundreds of times higher than the total amount on the coated stent for use in the proposed clinical trial.

Potential adverse events that may be unique to the paclitaxel drug coating are:

- Allergic/immunologic reactions 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, and thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in the vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/arthralgia
- Peripheral neuropathy

It is unlikely with the total dosages and the way paclitaxel is coated onto the stent and delivered in the vessel that the side effects associated with intravenous, high dose chemotherapy would occur. There may be other potential adverse events that are unforeseen at this time.

15.3 Risks associated with Participation in the Clinical Study

There may be additional risks linked to the procedure, and follow-up testing which are unforeseen at this time. All testings planned for the follow-up period are standard of care, with the exception of the quality of life questionnaires, which don’t cause any additional risk.

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 2-3 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.

15.4 Possible Interactions with Concomitant Medical Treatments

In addition to the aforementioned risks associated with the implantation of stents and the use of paclitaxel, the use of standard of care prolonged dual antiplatelet therapy after stent implantation may increase the risk of bleeding. Refer to the local package insert for further information on drug interactions and side effects associated with paclitaxel or antithrombotic/antiplatelet medications.

15.5 Risk Minimization Actions

Additional risks may exist. Risks can be minimized through compliance with this protocol, performing procedures in the appropriate hospital environment, adherence to subject selection criteria, close monitoring of the subject's physiologic status during research procedures and/or follow-ups and by promptly supplying BSC with all pertinent information required by this protocol.

15.6 Anticipated Benefits

Whether the subject receives the ELUVIA stent or another commercially available stent, they will receive an effective treatment of a narrowed upper leg artery and improvement in the symptoms of the peripheral artery disease.

Furthermore, medical science and future patients may benefit from the results of this study.

15.7 Risk to Benefit Rationale

The ELUVIA stent is a CE-marked device and has been proven to be suitable for its intended purpose. There are no unacceptable residual risks/intolerable risks and all applicable risks have been addressed through the provision of appropriate DFU. Evaluation of the risks and benefits that are expected to be associated with the use of the ELUVIA stent demonstrate that when used under the conditions intended, the benefits associated with the use of the ELUVIA stent should outweigh the risks.

16. STATISTICAL ANALYSIS

The details of all statistical analyses will be described in the Statistical Analysis Plan.

16.1 Primary Endpoint

The overall sample size is justified by hypothesis parameters and driven by the primary effectiveness endpoint to preserve adequate statistical testing power for the primary effectiveness endpoint.

16.1.1 Primary Effectiveness Endpoint

The 12-month primary patency is chosen to be assessed for the primary effectiveness endpoint. The goal is set to demonstrate that the primary patency for the ELUVIA treatment group (i.e. Test) is superior to the Self Expanding Bare Nitinol Stents treatment group (i.e. Control) through 12 months post-procedure. For the definition of primary patency, refer to section 8.1.

A Hypotheses

The primary effectiveness hypothesis to be tested is that the 12-month primary patency in the Test Group is superior to the Control Group at one-sided significance level of 2.5%.

The null hypothesis (H_0) states that there is no treatment effect between Test vs. Control as opposed to the alternative hypothesis (H_1) which states that there is a treatment effect. The hypotheses inequalities are shown below:

H_0: Pt - Pc ≤ 0

H_1: Pt - Pc > 0 (superior)

where Pt and Pc are the 12-month primary patency for Test and Control, respectively.

B Sample Size

The primary effectiveness endpoint drives the overall sample size. Approximately 750 subjects are planned to be enrolled. The sample size justification is based on the following assumptions:

- Expected ELUVIA (Test) 12-month primary patency = 85%
- Expected Self Expanding Bare Nitinol Stents (Control) 12-month primary patency rate = 75%
- Test significance level (α) = 2.5% (1-sided)
- Power ($1-\beta$) ≥ 85%
- Expected rate of attrition in 12 months ≤ 16%

With a sample size allocation (Test vs. Control) of 2 to 1, a minimum of 630 evaluable subjects in total (ideally 420 in the Test Group and 210 in Control Group) will be required at 12 months to provide at least 85% power under a one-sided 2.5% significance level.

The trial will demonstrate 10% treatment effect which represents 7% observed advance. Assuming a 12-month primary patency of 75.2% (158/210) is observed for Self Expanding Bare Nitinol Stents, a minimum of 82.1% (345/420) for ELUVIA will be required to claim superiority.

Taking into account the assumed attrition rate of 16%, this amounts to the enrollment of approximately 750 subjects

C Statistical Methods

A superiority test for the difference in 12-month primary patency will be used to assess the effectiveness hypotheses. The p-value and/or one-sided lower 97.5% confidence interval will be constructed based on statistics under this approach.

D Success Criteria

The following success criteria are defined for the study.

ELUVIA will be concluded to be superior to Self-Expanding Bare Nitinol Stents for device effectiveness if the one-sided lower 97.5% confidence bound on the difference between treatment groups (Test minus Control) in 12-month primary patency is greater than zero. This corresponds to the p-value less than 0.025.

If the primary effectiveness endpoint is met, the study will be considered a success.General Statistical Methods

16.1.2 Analysis Sets

The as-randomized (i.e. intent-to-treat or ITT) population will be the primary analysis set for assessing the primary effectiveness endpoint. The per-protocol and/or the as-treated population will be assessed for reference.

For the as-randomized analysis, all subjects who sign the written ICF and are randomized in the trial will be included in the analysis population, regardless of whether the subjects receive the assigned treatment. For the per-protocol analysis, only randomized subjects who receive the assigned treatment will be included in the analysis population. For as-treated analysis, all subjects in the per-protocol population will be included based on the actual Test or Control device that each subject received (i.e. including cross-over subjects).

16.1.3 Randomization Scheme

Randomization to treatment will be stratified by study site and lesion length. A computer generated list of random treatment allocations (i.e., a randomization schedule) will be used to assign subjects to treatments in a 2:1 ratio of Test Group to Control Group by lesion length (i.e. ≤110 mm vs. >110 mm) for each study site. This list will be specific to the subject's site. Random permuted blocks of varying sizes will be employed to ensure approximate balance of treatment allocation within each stratum.

16.1.4 Control of Systematic Error/Bias

Selection of subjects will be made from the Investigators' general or professional referral population. All subjects meeting the inclusion/exclusion criteria and who have signed the protocol-specific ICF will be eligible for enrollment in the trial. Consecutively eligible subjects should be enrolled into the trial to minimize selection bias. Study subjects will be randomly assigned to a treatment group within the investigational site. In determining subject eligibility

for the study, the investigator's assessment of imaging will be used. However, the Angiographic Core Laboratory will independently analyze the angiograms and the data obtained from the core laboratory will be used for analyses. An independent CEC composed of medical experts will adjudicate safety assessments, as defined in the CEC Charter.

16.1.5 Number of Subjects per Investigative Site

Study sites will not be allowed to randomize more than 10% (N=75) of the total number of randomized subjects without prior approval from the sponsor. No study site will be allowed to enroll more than 20% (N=150) of the total number of randomized subjects.

16.2 Baseline Data Analyses

Baseline covariates will be summarized for this study. Subject baseline demographics and clinical characteristics, site-reported and core lab reported lesion characteristics, procedure assessment, device information, and medication usage will be summarized using descriptive statistics. The analysis unit may be (but will not be limited to) by subject, lesion, procedure, or device.

The selected baseline covariates may be compared for 'like-to-like' in the Test Group verses the Control Group with appropriate statistical tests for discrete and continuous variables.

16.2.1 Secondary Endpoint and Additional Endpoints

The secondary endpoint and additional endpoints refer to (but are not limited to) health economics, technical/procedural success, safety/effectiveness endpoints, stent fracture, any type of ADE rates, survival rates, distribution of Rutherford classification, hemodynamic improvement at time points that data is collected.

No formal tests of hypotheses are proposed for the secondary endpoint and additional endpoints. Statistical comparisons may be performed for exploratory purposes. No formal inferences are planned on the secondary endpoint and additional endpoints and therefore alpha-adjustments for multiple comparisons will not be used.

16.2.2 Interim Analyses

No formal interim analyses are planned for the purpose of stopping this study early for declaring effectiveness or for futility.

16.2.3 Subgroup Analyses

Primary endpoint, secondary endpoint and/or additional endpoints will be summarized and treatment groups may be compared in each subgroup identified by the following categories (but not limited to):

- Region
- Race
- Gender (male vs. female)
- Age (≥ 65 and <65)

- Diabetic status (medically-treated vs. non-diabetic)
- Lesion characteristics (vessel diameter/lesion length)
- Stent matrix (stent diameter/length)
- Subjects treated with single stent/multiple stents (e.g. overlapping)
- Other significant predictors identified by regression models

No formal tests of hypotheses are proposed for subgroups and therefore alpha-adjustment for multiple comparisons is not required.

16.2.4 Justification of Pooling

The poolability analysis regarding the primary endpoint across sites will be assessed. Due to the 2:1 randomization scheme using random permuted blocks employed within each site, there will be at least 2 subjects from the Test Group and one subject from the Control Group. Therefore the poolability method is described as below.

The sites with enrollment of 6 subjects or more are reported individually.

The sites with enrollment of 5 or less subjects are pooled into super-sites according to their geographical closeness so that the combined super-sites would have 6 or more enrolled subjects. If a super-site has 6 or more subjects and at least 2 subjects in each treatment group, the pooling of this super-site should stop and the pooling of the next super-site should start.

If the p-value of poolability test in the logistic regression model for the primary endpoint is > 0.15, the treatment effect will be presented for overall across all sites. If the p-value is $\leq$ 0.15, the treatment effect will be presented by each site or super-site in addition to the overall across all sites.

16.2.5 Sensitivity Analysis for Missing Data

Sensitivity analyses for the primary effectiveness endpoint assessment will be conducted to assess the impact of missing data on the result's robustness. In addition to the use of the worst-case analysis, the tipping point analysis will be performed for the ITT analysis set to consider all combinations of present/absent for all subjects with missing primary outcome in the Test Group and the Control Group.

16.2.6 Multivariable Analyses

Univariate and multivariable analyses will be performed to assess the effect of potential predictors for the primary effectiveness endpoint in a logistic regression model. Clinically meaningful baseline covariates will be selected in the regression model. The study is not primarily designed to identify significant risk factors and all results should be interpreted with clinical meaningful aspects.

16.2.7 Analysis Software

All statistical analyses will be performed and validated by the independent CRO using the Statistical Analysis Software (SAS), version 9.2 or later (Copyright © 2002-2010 by SAS

Institute Inc., Cary, North Carolina 27513, USA. All rights reserved). BSC will review statistical reports.

16.2.8 Changes to Planned Analyses

Any changes to the planned statistical analyses made prior to performing the primary analyses (i.e. unblinding) will be documented in an amended Statistical Analysis Plan approved prior to performing the primary hypotheses testing. Changes from the planned statistical methods after performing the analyses will be documented in the clinical study report along with a reason for the deviation.

17. ETHICAL CONSIDERATIONS

17.1 Regulation Statement

This study will be performed in accordance with the World Medical Association Declaration of Helsinki, ISO 14155:2011(E) and all local legal and regulatory requirements.

In addition to following the governing regulations, any additional requirements of the individual study site's Ethics Committee and Regulatory Authority will also be followed by the study site(s) where applicable.

Ethics Committee and where applicable Regulatory Authority approval for the study is required prior to beginning the study. A copy of the approvals must be sent to the sponsor prior to enrolling the first subject.

The study will be publicly registered prior to first enrollment in accordance with the 2007 Food and Drug Administration Amendments Act (FDAAA) and Declaration of Helsinki on http://clinicaltrials.gov (PL 110-85, Section 810(a)).

17.2 Recruitment and Consent

This study is to be performed in accordance with all applicable data protection laws. All data and information concerning subjects and their participation in this study are considered confidential by the sponsor and its designees. Only authorized Investigators and Sponsor or designated personnel will have access to confidential records. The Ethics Committee and other regulatory authorities also have the right to inspect and copy records pertinent to the study. All public reporting of the results of the study will eliminate identifiable references to subjects.

The Investigator, or an individual designated by the investigator, must obtain written informed consent from the eligible subject prior to the first study-specific procedure using the most recent approved informed consent document.

The process of obtaining informed consent must be consistent with the Declaration of Helsinki. The study subject must be given the opportunity to ask questions to, and receive answers from, the investigator or study personnel prior to signing the consent document.

17.3 Investigator Responsibilities

The Principal Investigator of an investigational site is responsible for ensuring that the study is conducted in accordance with the Clinical Study Agreement, the investigational plan/protocol, ISO 14155, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing EC, and prevailing local and/or country laws and/or regulations, whichever affords the greater protection to the subject.

The Principal Investigator's responsibilities include, but are not limited to, the following.

- Prior to beginning the study, sign the Clinical Study Agreement and Protocol Signature page documenting his/her agreement to conduct the study in accordance with the protocol.
- Provide his/her qualifications and experience to assume responsibility for the proper conduct of the study and that of key members of the center team through up-to-date curriculum vitae or other relevant documentation and disclose potential conflicts of interest, including financial, that may interfere with the conduct of the clinical study or interpretation of results.
- Make no changes in or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency; document and explain any deviation from the approved protocol that occurred during the course of the clinical investigation.
- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical-investigation-related records are retained per requirements.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Record, report, and assess (seriousness and relationship to the device/procedure), per protocol requirements, every adverse device effect and observed device deficiency.
- Report to the sponsor, per the protocol requirements, all device deficiencies that could have led to a SADE.
- Report to the EC any SADEs and device deficiencies that could have led to a SADE, if required by the national regulations or this protocol or by the EC, and supply the sponsor with any additional requested information related to the safety reporting of a particular event.
- Maintain the device tracking of the test and control devices, ensuring that the device is used only by authorized/designated users and in accordance with this protocol and instructions/directions for use.
- Allow the sponsor to perform monitoring and auditing activities, and be accessible to the monitor and respond to questions during monitoring visits.
- Allow and support regulatory authorities and the EC when performing auditing activities.

- Ensure that informed consent is obtained in accordance with applicable laws, this protocol and local EC requirements.
- Provide adequate medical care to a subject during and after a subject's participation in the clinical study in the case of adverse events, as described in the ICF.
- Inform the subject of the nature and possible cause of any adverse events experienced.
- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded clinical investigations, as needed.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Ensure that, if appropriate, subjects enrolled in the clinical investigation are provided with some means of showing their participation in the clinical investigation, together with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided).
- Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.
- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical investigation while fully respecting the subject's rights.
- Ensure that an adequate investigational site team and facilities exist and are maintained and documented during the clinical investigation.
- Ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented, where applicable.

17.3.1 Delegation of Responsibility

When specific tasks are delegated by an investigator, including but not limited to conducting the informed consent process, the investigator is responsible for providing appropriate training and adequate supervision of those to whom tasks are delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

17.4 Ethics Committee

Prior to gaining Approval-to-Enroll status, the investigational site will provide to the sponsor documentation verifying that their EC is registered or that registration has been submitted to the appropriate agency, as applicable according to national/regulatory requirements.

A copy of the written EC and where appropriate Regulatory Authority approval of the protocol (or permission to conduct the study) and Informed Consent Form, must be received by the

sponsor before recruitment of subjects into the study. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Annual EC approval and renewals will be obtained throughout the duration of the study as required by local/country or EC requirements. Copies of the Investigator's reports and the EC continuance of approval must be provided to the sponsor.

17.5 Sponsor Responsibilities

All information and data sent to the sponsor concerning subjects or their participation in this study will be considered confidential by the sponsor and will be kept confidential in accordance with all applicable laws and regulations. Only authorized sponsor personnel and/or a sponsor representative including Contract Research Organization (CRO), will have access to these confidential records. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study. Study data collected during this study may be used by the sponsor for the purposes of this study, publication, and to support future research and/or other business purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products and procedures. All data used in the analysis and reporting of this study or shared with a third-party researcher will be without identifiable reference to specific subjects.

Information received during the study will not be used to market to subjects; subject names will not be placed on any mailing lists or sold to anyone for marketing purposes.

17.5.1 Role of Sponsor Representatives

Sponsor personnel can provide technical support to the investigator and other Health Care Personnel (collectively HCP) as needed during stent implant and testing required by the protocol during the index procedure. Support may include HCP training, addressing HCP questions, or providing clarifications to HCPs concerning the operation of the test device.

Sponsor personnel will not do the following:

- Practice medicine
- Provide medical diagnosis or treatment to subjects
- Discuss a subject's condition or treatment with a subject
- Independently collect critical study data (defined as primary or secondary endpoint data)
- Enter data in electronic data capture systems or on paper case report forms

18. REIMBURSEMENT AND COMPENSATION FOR SUBJECTS

18.1 Subject Reimbursement

Travel expenses incurred by subjects as a result of participation in the study will be reimbursed if requested in accordance with pertinent country laws and regulations and per the study site's regulations.

18.2 Compensation of Injury

The sponsor has insurance, in accordance with national regulations, covering the costs of treatment of subjects in the event of study related injuries.

19. ADMINISTRATIVE ASPECTS AND PUBLICATION

19.1 Handling and Storage of Data and Documents

The investigators must maintain adequate and accurate records to document the conduct of the study and substantiate the study data. These documents include those required by applicable regulations, and the subjects' source documents, as described below.

Regulatory documents are those documents that individually and collectively permit evaluation of the study compliance with applicable regulations and the quality of the data produced.

These documents will be filed in an Investigator Study File provided by the sponsor or designee. This file shall be used to facilitate and ensure filing of all relevant regulatory documents during and after the study. The investigator will be responsible for keeping the Investigator's Study File updated and ensuring that all required documents are filed. The file will be inspected during monitoring visits.

Source documents are original hospital records, clinical charts, screening log, subject identification lists, enrolment logs, original laboratory reports, memoranda, pharmacy dispensing records, recorded data from automated instruments, transcriptions certified after verification as being accurate, microfiches, photographic negatives, microfilm, magnetic or electronic media, x-rays, subject's files, and records kept at pharmacy, laboratories and medico-technical departments involved in the study. The investigator must maintain source documents for each subject in the study.

All information recorded on the CRFs must be traceable to these source documents. The investigator shall arrange for the retention of all study documents and records, including subject records, CRFs, device inventory/accountability logs, signed informed consent forms and the subject identification list, after completion or discontinuation of the study for the minimum period as required per local regulation.

19.2 Data Collection and Case Report Forms (CRF)

Clinical data are collected at designated time points throughout the study. Electronic Case Report Forms (eCRFs) will be used to collect all patient data during the course of the study. eCRFs must be fully completed for each subject and signed by the Investigator when complete. Data may be stored in a secure, password-protected database which will be backed up periodically. Data will be reviewed using programmed and manual data checks.

Data queries will be made available to study sites for resolution. Study management reports may be generated by the sponsor (or delegate) to monitor data quality and study progress. At the end of the study, the data will be frozen and retained by the sponsor for a period of five (5) years, or as required by local regulation.

Good Clinical Practice Guidelines require that Investigators maintain information in the study subject's medical records that corroborate data collected in the CRFs.

The Investigator or designated individual shall be responsible for recording all study data on the CRFs provided by the sponsor. The Investigator is required to sign the CRF on the appropriate page(s) to verify that he/she has reviewed and agrees with the recorded data.

The Investigator will allow the monitor and/or representative of the Sponsor, and any regulatory body to review and inspect the study files, subject CRFs, subject medical records and other related study documents as required. Completed CRFs will be verified by the appointed monitor at the investigational site at regular intervals throughout the study. Missing or unclear data will be investigated by the monitor and will be retrieved and clarified by study personnel as necessary throughout the study. The sponsor or their authorized representative may request additional documentation from the investigator such as physician procedure notes or physician written summaries when adverse events are observed and reported.

19.3 Deviations

The investigator is not allowed to deviate from the Clinical Investigational Plan, except to maintain the subject's rights, protect the life and physical well-being of a subject in an emergency, or the scientific integrity of the investigation. All protocol deviations shall be documented and a justification for any missed assessments shall be provided on the Protocol Deviation Case Report Form.

The sponsor (or delegate) is responsible for analyzing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g. amend the Clinical Investigational Plan, conduct additional training, or terminate the investigation). Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the investigator and site, and in some cases, necessitate suspending enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study. Sponsor (or delegate) will provide site-specific reports to investigators summarizing information on deviations that occurred at the investigational site on a periodic basis.

19.4 CIP Revisions or Amendments

During the course of the study, a revision or an amendment to the Clinical Investigational Plan may be necessary. Any revision or amendment, including justification for the modification, must be submitted to and approved by the study site's Ethics Committee and if applicable to the relevant Regulatory Authority according to local requirements prior to implementation of the amendment, unless the modifications increase Subject safety.

Any revisions or amendment(s) that affect the informed consent form require a revised, Sponsor and Ethics Committee approved informed consent form, before changes in study procedures are implemented. These requirements should in no way prevent any immediate action from being taken by the Investigator or by the Sponsor to preserve the safety of any Subjects included in the study, as necessary. If an immediate change to the Clinical

Investigational Plan is felt to be necessary by the Investigator and is implemented by him/her for safety reasons, the Sponsor, and EC if required, should be immediately notified.

19.5 Annual Progress Report

The sponsor/investigator will submit a summary of the progress of the study to the involved ethics committees once a year or according to the national / local requirements.

Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the study, serious adverse device effects, UADEs, device deficiencies, protocol deviations, revisions, and amendments.

19.6 End of Study Report

The sponsor (or delegate) will notify the involved Ethics Committees and where appropriate the Regulatory Authority of the end of the study within a period of 90 days. The end of the study is defined as the last subject's last visit.

In case the study is ended prematurely, the sponsor (or delegate) will notify the involved Ethics Committees and where appropriate the Regulatory Authorities within 15 days, including the reasons for the premature termination.

If required by the national regulations, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the involved Ethics Committee and, if applicable, the Regulatory Authority within one year from the end of the study.

19.7 Public Disclosure and Publication Policy

In accordance with the sponsor's Corporate Policy on the Conduct of Human Subject Research, the sponsor requires disclosure of its involvement as a sponsor or financial supporter in any publication or presentation relating to a sponsor's study or its results. In accordance with the sponsor's Corporate Policy for the Conduct of Human Subject Research, the sponsor will submit study results for publication (regardless of study outcome) following the conclusion or termination of the study. The sponsor adheres to the Contributorship Criteria set forth in the Uniform Requirements of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org). In order to ensure the public disclosure of study results in a timely manner, while maintaining an unbiased presentation of study outcomes, sponsor personnel may assist authors and investigators in publication preparation provided the following guidelines are followed.

- All authorship and contributorship requirements as described above must be followed.
- Sponsor involvement in the publication preparation and the sponsor Publication Policy should be discussed with the Coordinating Principal Investigator(s) and/or Executive Committee at the onset of the project.
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

Publication status will be posted to the pertinent study listing on clinicaltrials.gov.

The study data, analytic methods, and study materials for this clinical trial may be made available to other researchers in accordance with the Boston Scientific Data Sharing Policy (https://www.bostonscientific.com/).

20. MONITORING

It is the responsibility of the Sponsor to ensure proper monitoring of this clinical study per regulations. Trained Sponsor personnel or delegates appointed by the Sponsor may perform study monitoring at the study site in order to ensure that the study is conducted in accordance with the Clinical Investigational Plan, the Clinical Study Agreement, and applicable regulatory and local requirements. The Sponsor, or delegates, must therefore be allowed access to the subjects' case histories (clinic and hospital records, and other source data/ documentation) upon request as per the consent form, Research Authorization (where applicable) and Clinical Study Agreement. The principal investigator should also be available during monitoring visits.

20.1 Monitoring Visits

Monitoring visits may be conducted periodically to assess site study progress, the investigator's adherence to the Clinical Investigational Plan, regulatory compliance, maintenance of records and review of source documents against subject CRFs. Monitors review site regulatory and study compliance by identifying findings of non-compliance and communicating those findings along with recommendations for preventative/corrective actions to site personnel. Monitors may work with study personnel to determine appropriate corrective action recommendations and to identify trends within the study or at a particular site.

Frequency of monitoring visits may be based upon subject enrollment, duration of the study, study compliance, number of adverse events, number of deviations, findings from previous monitoring visits and any suspected inconsistency in data that requires investigation. Regulatory documents may be reviewed at each study site. Monitoring for the study will be done in accordance to the study monitoring plan. Monitoring will be based on the Key Risk Indicators (Risk Based Monitoring) as described in the Risk Based Monitoring Plan.

21. ABBREVIATIONS AND DEFINITIONS

21.1 Abbreviations

Abbreviation	Terminology
ABI	Ankle Brachial Index
ACC/AHA	American College of Cardiology/American Heart Association
ADE	Adverse Device Effect
AE	Adverse Event
BSC	Boston Scientific Corporation
CE	Conformité Européenne (meaning European Conformity)
CEC	Clinical Events Committee
CIN	Contrast-Induced Nephropathy
CRF	Case Report Form
CVA	Cerebrovascular Accident
DES	Drug Eluting Stent
DUS	Duplex Ultrasound
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDAAA	Food and Drug Administration Amendments Act
ICF	Informed Consent Form
ITT	Intent to Treat
MAE	Major Adverse Event
PPA	Proximal Popliteal Artery
PSVR	Peak Systolic Velocity Ratio
PTA	Percutaneous Transluminal Angioplasty

Abbreviation	Terminology
QA	Quantitative Angiography
RCC	Rutherford-Becker clinical classification
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SDS	Stent Delivery System
SFA	Superficial Femoral Artery
TBI	Tibial Brachial Index
TLR	Target Lesion Revascularization
TVR	Target Vessel Revascularization
UADE	Unanticipated Adverse Device Effect
VIVA	Vascular InterVentional Advances
WIQ	Walking Impairment Questionnaire
6MHW	Six Minute Hall Walk

21.2 Definitions

Term	Definition
AMPUTATION	• Major Amputation: amputation of the lower limb at the ankle level or above. • Minor Amputation: amputation of the lower limb below the ankle level, i.e. forefoot or toes.
ANKLE-BRACHIAL INDEX (ABI)	The ratio between the systolic pressure measured at the ankle and the systolic pressure measured in the arm as follows: • Ankle: The systolic pressure will be measured in the target limb at the arteria dorsalis pedis and/or the arteria tibialis posterior. If both pressures are measured, the highest pressures will be used for the ABI calculation. • Brachial: The systolic pressure will be measured in both arms, and the highest of both pressures will be used for the ABI calculation.
ASSISTED PRIMARY PATENCY	Percentage (%) of lesions without TLR and those with TLR (not due to complete occlusion or by-pass) that reach endpoint without restenosis.
CALCIFICATION	Readily apparent densities seen within the artery wall and site of lesion as an x-ray-absorbing mass.
CEREBRO-VASCULAR ACCIDENT (CVA)	An acute symptomatic episode of neurological dysfunction attributed to a vascular cause lasting more than 24 hours or lasting 24 hours or less with a brain imaging study or autopsy showing infarction.
COMPLICATION	An undesirable clinical event that results in death, injury, or invasive intervention. Complications may include, but are not limited to perforation, occlusion, intimal flap, dissection, loss of side branch, distal embolization, hypotension, hematoma, arrhythmias, etc. Complications may or may not be related to the device(s).

Term	Definition
DEATH	All deaths are considered cardiac unless an unequivocal non-cardiac cause can be established. Specifically, an unexpected death in subjects with coexisting potentially fatal non-cardiac diseases (e.g. Cancer, infection) should be classified as cardiac. All death events will be submitted to CEC and will be categorized as: Cardiac death: any death due to immediate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia). Unwitnessed death and death of unknown cause will be classified as cardiac death. This includes all procedure related deaths including those related to concomitant treatment. Vascular death: death due to cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause**.** Non-cardiovascular death: any death not covered by the above definitions, including death due to infection, sepsis, pulmonary causes, accident, suicide, or trauma.
DIAMETER STENOSIS	The maximal narrowing of the target lesion relative to the reference vessel diameter.
DISSECTION-NHLBI GRADE TYPES	Type A- Small radiolucent area within the lumen of the vessel disappearing with the passage of the contrast material. Type B- Appearance of contrast medium parallel to the lumen of the vessel disappearing within a few cardiac cycles. Type C- Dissection protruding outside the lumen of the vessel persisting after passage of the contrast material. Type D- Spiral shaped filling defect with or without delayed run-off of the contrast material in the antegrade flow. Type E- Persistent luminal filling defect with delayed run-off of the contrast material in the distal lumen. Type F- Filling defect accompanied by total vessel occlusion.
DISTAL EMBOLIZATION	Migration of a filling defect, or thrombus, to distally occlude the target vessel or one of its branches.

Term	Definition
EQ-5D-5L™	Descriptive system of health-related quality of life states consisting of the EQ-5D descriptive system and the EQ visual analogue scale (EQ VAS). The EQ-5D consists of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which can take one of five responses. The responses record five levels of severity (no problems/slight problems/moderate problems/severe problems/extreme problems) within a particular EQ-5D dimension. The EQ VAS records the respondent's self-rated health on a vertical, visual analogue scale where the endpoints are labelled 'Best imaginable health state' and 'Worst imaginable health state'. This information can be used as a quantitative measure of health outcome as judged by the individual respondents.
HEMATOMA	A localized swelling filled with blood resulting from a break in a blood vessel.
HEMODYNAMIC IMPROVEMENT	Improvement of ABI by ≥0.1 or to an ABI ≥ 0.90 as compared to the pre-procedure value without the need for repeat revascularization.
HYPOTENSION	Systolic blood pressure < 80 mmHg lasting more than 30 minutes or requiring intervention (e.g. pacing, IABP, intra venous vasopressors to sustain systolic blood pressure). This excludes transient hypotension or vagal reactions, which are self-limited or readily reversible.
INTIMAL FLAP	An extension of the vessel wall into the arterial lumen.
LESION LENGTH	Measured as the distance from the proximal shoulder to the distal shoulder of the lesion, in the view that demonstrates the stenosis in its most elongated projection.
MAJOR ADVERSE EVENT (MAE)	MAE is defined as all causes of death, target limb major amputation and/or Target Lesion Revascularization (TLR)
PERFORATION	Perforations are classified as follows: ***Angiographic perforation*:** perforation detected by the clinical site or Angiographic Core Laboratory at any point during the procedure. ***Clinical perforation*:** perforation requiring additional treatment (including efforts to seal the perforation), or resulting in significant hemodynamic compromise, abrupt closure, or death.

Term	Definition
PRIMARY PATENCY	Percentage (%) of lesions that reach endpoint without a hemodynamically significant stenosis on DUS and without TLR or, bypass of the target lesion.
PRIMARY SUSTAINED CLINICAL IMPROVEMENT	Endpoint determined to be a success when there is an improvement in Rutherford classification of one or more categories as compared to pre-procedure without the need for repeat TLR.
PROCEDURAL SUCCESS	Technical success with no MAEs noted within 24 hours of the index procedure.
PSEUDO-ANEURYSM	An encapsulated hematoma in communication with an artery.
REPEAT INTERVENTION (PERCUTANOUS AND/OR SURGERY)	Either repeat percutaneous transluminal angioplasty (PTA) or artery bypass surgery, performed subsequently to the subject leaving the cath lab after the index procedure.
REFERENCE VESSEL DIAMETER (RVD) OF NORMAL ARTERY SEGMENT	Angiographic measurement of the artery proximal and/or distal to the lesion intended for treatment.
RESTENOSIS	DUS systolic velocity ratio (SVR) >2.4 suggest stenosis >50%.

<table>
<tr><th>Term</th><th>Definition</th></tr>
<tr><td>RUTHERFORD / BECKER CLASSIFICATION</td><td>
<table>
<tr><th>Category</th><th>Clinical Description</th><th>Objective Criteria</th></tr>
<tr><td>0</td><td>Asymptomatic</td><td>Normal Treadmill /stress test</td></tr>
<tr><td>1</td><td>Mild claudication</td><td>Completes treadmill exercise; ankle pressure (AP) after exercise <50mm Hg, but >25 mm Hg less than BP</td></tr>
<tr><td>2</td><td>Moderate claudication</td><td>Between categories 1 and 3</td></tr>
<tr><td>3</td><td>Severe claudication</td><td>Cannot complete treadmill exercise and AP after exercise <50 mm Hg</td></tr>
<tr><td>4</td><td>Ischemic rest pain</td><td>Resting AP <40 mm Hg, flat or barely pulsatile ankle or metatarsal pulse volume recording (PVR); toe pressure (TP) <30 mm Hg</td></tr>
<tr><td>5</td><td>Minor tissue loss – nonhealing ulcer, focal gangrene with diffuse pedal edema</td><td>Resting AP <60 mm Hg, ankle or metatarsal (MT) PVR flat or barely pulsatile; TP <40 mm Hg</td></tr>
<tr><td>6</td><td>Major tissue loss – extending above TM level</td><td>Same as Category 5</td></tr>
</table>
</td></tr>
<tr><td>SECONDARY SUSTAINED CLINICAL IMPROVEMENT</td><td>Endpoint determined to be a success when there is an improvement in Rutherford classification of one or more categories as compared to pre-procedure including those subjects with repeat TLR.</td></tr>
<tr><td>SOURCE DATA</td><td>All information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the trial. Source data are contained in the source documents (original records or certified copies).</td></tr>
<tr><td>SOURCE DOCUMENT</td><td>Original documents, data or records.
Examples: Hospital records, laboratory notes, device accountability records, photographic negatives, radiographs, records kept at the investigation site, at the laboratories and at the medico-technical departments involved in the clinical investigation.</td></tr>
</table>

Term	Definition
STENT FRACTURE	A break in one or more places of the stent. The following definitions will be used to determine the type and extent of stent fracture (to be assessed by the x-ray core laboratory):[3] • Grade 0: No Strut fractures • Grade I: single strut fracture • Grade II: multiple strut fractures • Grade III: stent fracture(s) with preserved alignment of the components • Grade IV: stent fracture(s) with mal-alignment of the components • Grade V: Stent fracture(s) in a trans-axial spiral configuration
STENT THROMBOSIS	The occurrence of either of the following: 1. Angiographic documentation (or any other imaging modality if angiography not available) of an acute, complete occlusion of a previously successfully treated lesion and/or 2. Angiographic documentation (or any other imaging modality if angiography not available) of a flow-limiting thrombus within, or adjacent to, a previously successfully treated lesion *Acute* stent thrombosis is defined as occurring ≤24 hours following the clinical study procedure. *Subacute* stent thrombosis is defined as occurring >24 hours to ≤30 days following the clinical study procedure. *Late* stent thrombosis is defined as >30 days to 365 days following the clinical study procedure. *Very late* stent thrombosis is defined as >365 days following the clinical study procedure.
TARGET LESION	A target lesion is identified as a clinical study lesion intended to be treated with a test or control device during the index procedure.

Term	Definition
TARGET LESION REVASCULARIZATION (TLR)	Any surgical or percutaneous intervention to the target lesion(s) after the index procedure when one of the following situations is present: • A target lesion revascularization will be considered clinically-driven if it occurs within 5 mm proximal or distal to the original treatment segment with diameter stenosis ≥50% by quantitative angiography (QA) and the subject has recurrent symptoms (≥ 1 change in Rutherford Classification or associated with decreased ABI/TBI of ≥ 20% or ≥ 0.15 in the treated segment. TBI allowed in cases of incompressible vessels.) • A target lesion revascularization for an in-lesion diameter stenosis less than 50% might also be considered a MAE by the CEC if the subject has recurrent symptoms (≥ 1 change in Rutherford Classification or associated with decreased ABI/TBI of ≥ 20% or ≥ 0.15 in the treated segment. TBI allowed in cases of incompressible vessels.)
TARGET VESSEL	Target vessel is defined as the vessel containing the target lesion(s). If the target lesion is entirely within the right superficial femoral artery, then the target vessel is the right superficial femoral artery. If the target lesion extends from the right superficial femoral artery into the right proximal popliteal artery, then both the right superficial femoral artery and right proximal popliteal artery would be considered part of the target vessel.
TARGET VESSEL REVASCULARIZATION (TVR)	Any surgical or percutaneous intervention to the target vessel(s) after the index procedure when one of the following situations is present: • A target vessel revascularization will be considered as clinically-driven if the culprit lesion stenosis is ≥50% by QA and the subject has recurrent symptoms (≥ 1 change in Rutherford Classification or associated with decreased ABI/TBI of ≥ 20% or ≥ 0.15 in the treated segment. TBI allowed in cases of incompressible vessels.)

Term	Definition
TRANSATLANTIC INTER-SOCIETAL CONSENSUS (TASC) LESION GUIDELINES	Type A lesion: • Single stenosis ≤ 10 cm in length. • Single occlusion ≤ 5 cm in length. Type B lesion: • Multiple lesions (stenoses or occlusions), each ≤ 5cm • Single stenosis or occlusion ≤ 15cm not involving the infra geniculate popliteal artery • Single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass • Heavily calcified occlusion ≤ 5cm in length • Single popliteal stenosis Type C lesion: • Multiple stenoses or occlusions totaling > 15cm with or without heavy calcification • Recurrent stenoses or occlusions that need treatment after two endovascular interventions Type D lesion: • Chronic total occlusions of the CFA or SFA (>20cm, involving the popliteal artery) • Chronic total occlusion of the popliteal artery and proximal trifurcation vessels
TECHNICAL SUCCESS	Delivery and deployment of the assigned study stent to the target lesion to achieve residual angiographic stenosis no greater than 30% assessed visually.
THROMBUS (ANGIOGRAPHIC)	Discrete, mobile intraluminal filling with defined borders with/without associated contrast straining; these are classified as either absent or present.
TOTAL OCCLUSION	Lesion with no flow; implies 100% diameter stenosis.
VASCULAR COMPLICATION	An occurrence of hematoma >5 cm, pseudoaneurysm, arteriovenous (AV) fistula, or need for vascular surgical repair.

Term	Definition
VESSEL PATENCY	Freedom from more than 50% stenosis based on duplex ultrasound (DUS) peak systolic velocity ratio (PSVR) comparing data within the treated segment to the proximal normal arterial segment. A PSVR > 2.4 suggests >50% stenosis. All DUS readings are assessed by an independent core lab.
WALKING IMPAIRMENT QUESTIONNAIRE (WIQ)	The WIQ is a functional-assessment questionnaire that evaluates walking ability with regard to speed, distance and stair climbing ability as well as the reasons that walking ability might be limited. Range of scores is between 0% and 100% with 100% being the best and 0% being the worst score.

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