A Randomized Trial comparing the Drug-Eluting Stent (DES) Below-the-Knee (BTK) Vascular Stent System (DES BTK Vascular Stent System) vs Percutaneous Transluminal Angioplasty (PTA) Treating Infrapopliteal Lesions in Subjects With Critical Limb Ischemia

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Primary objective: To demonstrate a superior patency rate and acceptable safety rates in below the knee arteries with lesions treated with the DES BTK Vascular Stent System vs percutaneous transluminal angioplasty. (PTA). Secondary objective: To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Vascular therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON56263

Source
ToetsingOnline

Brief title
Saval Pivotal Trial

Condition

- Vascular therapeutic procedures

Synonym
Critical Limb Ischemia, peripheral artery disease

Research involving
Human

Sponsors and support

Primary sponsor: Boston Scientific Cooperation International
Source(s) of monetary or material Support: Industry

Intervention

Keyword: Critical Limb Ischemia, DES BTK Vascular Stent System, Infrapopliteal Lesions, Percutaneous Transluminal Angioplasty

Outcome measures

Primary outcome

Primary Effectiveness Endpoint (Phase A RCT)

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 DES BTK treatment group is superior to the PTA treatment group at an overall one-sided significance level of 2.5%.

Primary vessel patency is defined as a binary endpoint to be determined via duplex ultrasound (DUS) measuring flow or no flow at the 12-month follow-up visit in the absence of clinically-driven target lesion revascularization (TLR) or bypass of the target lesion. All DUS readings will be assessed by an independent core laboratory.

Primary Safety Endpoint (Phase A RCT)

The primary safety endpoint assesses major adverse events (MAE) at 12 months post-procedure. This safety endpoint is designed to demonstrate that the

12-month MAE-free rate for the DES BTK treatment group is non-inferior to the PTA treatment group at an overall one-sided significance level of 2.5%.

A major adverse event is defined as the composite of:

• Above ankle amputation of the index limb

• Major re-intervention (ie, new bypass graft, jump/interposition graft, or thrombectomy/thrombolysis)

• Perioperative (30 day) mortality

Secondary outcome

Additional Endpoints Phase A:

• Primary and assisted-primary patency at 1, 6, 12, 24, and 36 months post-procedure

• Clinically-driven target lesion revascularization (TLR) rate at each time point

• Hemodynamic outcomes (changes in Ankle-Brachial Index [ABI] and/or Toe-Brachial Index [TBI]) at 6 and 12 months post procedure

• Wound assessment (changes in wound characteristics)

• Major amputation rate

• Change in Rutherford classification at 3, 6, 12, 24, and 36 months post procedure

• Quality of Life (QOL) changes at 1, 3, 6 and 12 months post procedure

• Adverse events (AEs) at each time point (to be classified as major, serious, non-serious, unanticipated, procedure-related and device-related)

• 30-day unplanned hospital readmission rate

Study description

Background summary

Critical limb ischemia is a debilitating disease, associated with poor clinical outcomes, a high rate of amputations, and overall decreased quality of life. Based on the significant clinical complications associated with bypass surgery, the presence of chronic total occlusions, the restenotic characteristics with PTA therapies, and the limitations of using coronary stents in BTK indications, the need for an alternative therapy exists.

The DES BTK Vascular Stent System aims to address these treatment gaps and clinical outcomes not adequately addressed by surgical bypass and/or PTA. The DES BTK Vascular Stent System was designed for the unique considerations of infrapopliteal disease, including long, tortuous lesions and the need for a mechanism of providing an anti-proliferative agent to calcified vessels. The DES BTK Vascular Stent System incorporates existing successful peripheral drug-eluting stent technology to treat a similar disease state below the knee.

Study objective

Primary objective: To demonstrate a superior patency rate and acceptable safety rates in below the knee arteries with lesions treated with the DES BTK Vascular Stent System vs percutaneous transluminal angioplasty. (PTA).

Secondary objective: To collect additional information on limb salvage and overall quality of life in this patient population.

Study design

The trial will be conducted in 1 phase.

Phase A is a global, pivotal, prospective, multicenter, 2:1 randomized controlled trial (RCT) evaluating the safety and effectiveness of the DES BTK Vascular Stent System compared to PTA for the treatment of lesions located in the arteries below the knee in subjects with CLI.

Intervention

Test device : The DES BTK Vascular Stent System for treatment of lesions in the infrapopliteal arteries.
Control device: Percutaneous Transluminal Angioplasty (PTA) balloon catheter.

For additional information please refer to the protocol (synopsis, page 18)

Study burden and risks

Subjects have to attend visits (screening, implantation of stent/PTA, follow up visits) and a variety
of tests will be done to check their health. These include medicine use/ medical history and physical assessment, blood tests, questionnaires, pregnancy testing, angiogram, x-ray of limb, ultrasound tests, ABI and TBI, wound assessment & image. Subjects must use a birth
control method.

Risks include: Allergic reaction (to drug/polymer, contrast, device or other), Amputation Bleeding/Hemorrhage, Death, Embolization (air, plaque, thrombus, device, tissue or other), Hematoma, Ischemia, Need for urgent intervention or surgery, Pseudoaneurysm formation, Renal insufficiency or failure, Restenosis of stented artery, Sepsis/infection, Thrombosis / Thrombus, Transient hemodynamic instability (hypotensive/hypertensive episodes), Vasospasm, Vessel injury, including perforation, trauma, rupture and dissection, Vessel occlusion. There are also risks associated with the Paclitaxel drug coating on the DES BTK stent: 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.

SOC antiplatelet medications is associated with the risk of bleeding. In general there are risks associated with the blood draws and X-ray and potential harm to the unborn child.

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Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Pre-procedure Inclusion Criteria
1. Subject is 18 years or older and has signed and dated the trial informed consent form (ICF). Note: For subjects in Japan who are less than 20 years of age, the subject*s legal representative must provide written informed consent in addition to the subject
2. Subject is willing and able to comply with the trial testing, procedures and follow-up schedule
3. Subject has chronic, symptomatic lower limb ischemia, determined by Rutherford categories 4 or 5 in the target limb, with wound(s) confined to toes/forefoot
4. Subject is a male or non-pregnant female. If female of child-bearing potential, and if sexually active must be using, or agree to use, a medically-

acceptable method of birth control as confirmed by the investigator

Intra-Procedure Inclusion Criteria
1. Stenotic, restenotic or occlusive target lesion(s) located in the tibioperoneal trunk, anterior tibial, posterior tibial and/or peroneal artery(ies).
• Target lesion(s) must be at least 4cm above the ankle joint
• A single target lesion per vessel, in up to 2 vessels, in a single limb
• Degree of stenosis >= 70% by visual angiographic assessment
• Reference vessel diameter (RVD) is between 2.5 - 3.25mm for phase A RCT
• Total target lesion length (or series of lesion segments) to be treated is <= 140mm for phase A RCT after DMC approval for stent overlap (Note: Lesion segment(s) must be fully covered with up to two DES BTK stents, if randomized to stent)
• Total target lesion length (or series of lesion segments) to be treated is <= 140mm for phase B non-randomized (Note: Lesion segment(s) must be fully covered with up to two DES BTK stents)

2. Target vessel(s) reconstitute(s) at or above the stenting limit zone (4cm above the ankle joint)
3. Target lesion(s) is located in an area that may be stented without blocking access to patent main branches
4. Treatment of all above the knee inflow lesion(s) is successful prior to treatment of the target lesion
5. Guidewire has successfully crossed the target lesion(s)

Exclusion criteria

Pre-Procedure Exclusion Criteria
1. Life expectancy <= 1year
2. Stroke <= 90 days prior to the procedure date
3. Prior or planned major amputation in the target limb
4. Previous surgery in the target vessel(s) (including prior ipsilateral crural bypass)
5. Previously implanted stent in the target vessel(s)
6. Failed PTA of target lesion/vessel <= 60 days prior to the procedure date
7. Renal failure as measured by a GFR <= 30ml/min per 1.73m2, measured <= 30 days prior to the procedure date
8. Subject has a platelet count <= 50 or >= 600 X 103/µL <= 30 days prior to the procedure date
9. NYHA class IV heart failure
10. Subject has symptomatic coronary artery disease (ie, unstable angina)
11. History of myocardial infarction or thrombolysis <= 90 days prior to the procedure date

12. Non-atherosclerotic disease resulting in occlusion (eg, embolism, Buerger*s disease, vasculitis)
13. Subject is currently taking Canagliflozin
14. Body Mass Index (BMI) <18
15. Active septicemia or bacteremia
16. Coagulation disorder, including hypercoagulability
17. Contraindication to anticoagulation or antiplatelet therapy
18. Known allergies to stent or stent components
19. Known allergy to contrast media that cannot be adequately pre-medicated prior to the interventional procedure
20. Known hypersensitivity to heparin
21. Subject is on a high dose of steroids or is on immunosuppressive therapy
22. Subject is currently participating, or plans to participate in, another investigational trial that may confound the results of this trial (unless written approval is received from the Boston Scientific study team),

Intra-procedure Exclusion Criteria
1. Angiographic evidence of intra-arterial acute/subacute thrombus or presence of atheroembolism
2. Treatment required in > 2 target vessels (Note: a target lesion originating in one vessel and extending into another vessel is considered 1 target vessel)
3. Treatment requires the use of alternate therapy in the target vessel(s)/lesion(s), (eg, atherectomy, cutting balloon, re-entry devices, laser, radiation therapy)
4. Aneurysm is present in the target vessel(s)
5. Extremely calcified lesions

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-04-2019
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	DES BTK Drug-Eluting Vascular Stent System
Registration:	No

Ethics review

Approved WMO Date:	24-08-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-11-2018
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL65790.056.18