Randomized Study of IN.PACT 014 Paclitaxel-Coated Percutaneous Transluminal Angioplasty Balloon Catheter vs. Optimal Percutaneous Transluminal Angioplasty for the treatment of chronic total occlusions in the infrapopliteal arteries.

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To assess the safety and efficacy of the paclitaxel drug-eluting balloon IN.PACT 014 versus conventional, optimal percutaneous transluminal angioplasty (PTA) for the treatment of patients with chronic total occlusions in the infrapopliteal arteries...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Arteriosclerosis, stenosis, vascular insufficiency and necrosis
Study type	Interventional

Summary

ID

NL-OMON46468

Source
ToetsingOnline

Brief title
IN.PACT BTK

Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
chronic total occlusions in the infrapopliteal arteries

Research involving
Human

Sponsors and support

Primary sponsor: Medtronic B.V.
Source(s) of monetary or material Support: industrie

Intervention

Keyword: Angioplasty Balloon, Paclitaxel, Randomized Controlled Trial

Outcome measures

Primary outcome

To assess the efficacy of the IN.PACT 014 by comparing the Late Lumen Loss (LLL) 9 months after the index procedure of the investigational product vs optimal (conventional) PTA

Secondary outcome

• Composite Safety Endpoint: A composite of freedom from device- and procedure-related mortality within 30 days, freedom from major target limb amputation and freedom from clinically-driven TLR within 9 months post-index procedure.

• Major Adverse Event (MAE) rate, defined as a composite of all-cause mortality, target limb major amputation and clinically-driven TLR through 3, 6, 9, 12, 24 and 36 months.

• Functional flow assessment at 3, 6, 9, 12 and 24 month, defined as absence of target lesion occlusion (no flow) assessed by duplex ultrasound.

• Death of any cause and cardiovascular related deaths through 3, 6, 9, 12 and 24 months.

• Rate of major target limb amputation through 30 days, 3, 6, 9 ,12 and 24

months.

• Rate of CD-TLR through 3, 6, 9, 12 and 24 months.

• Rate of Mechanically Driven TLR through 30 days.

• Rate of TLR through 3, 6, 9, 12 and 24 months.

• Rate of CD-TVR through 3, 6, 9, 12 and 24 months.

• Rate of TVR through 3, 6, 9, 12 and 24 months.

• Status of wound healing (completely healed - improvement - unchanged - worsened) at 30 days, 3, 6, 9, 12 and 24 months.

• Rate of thrombosis at the target lesion through 30 days, 3, 6, 9, 12 and 24 months.

• Device success (for investigational device only)

Device success is defined as successful drug delivery, balloon inflation, deflation and retrieval of the intact study device without burst below the rated burst pressure (RBP).

• Clinical success

Clinical success is defined as residual stenosis of <= 30% without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.

Study description

Background summary

Peripheral arterial disease (PAD) is a commonly occurring medical condition that involves atherosclerosis in vessels located outside the heart and brain. PAD affects an estimated 27 million adults in Europe and North America.Patients suffering from PAD generally experience a significant reduction in

health-related quality of life (QOL).
Patients with PAD tend to experience an increase in morbidity and a reduction in health status measures of health-related QOL. Potential consequences of lower extremity arterial disease include reduced mobility, limb pain, gangrene, and amputation, as well as increased mortality, amongst others. Critical limb ischemia (CLI) refers to severe persistent rest pain requiring treatment with analgesics, ulceration or gangrene on the distal extremity. PAD located below-the-knee is more likely to be diffuse and progressive than above-the-knee PAD, which is often characterized by multilevel disease and heavily calcified lesions. Patients often present with symptoms of CLI as opposed to claudication. Comorbidities such as diabetes and renal failure occur rather frequently alongside PAD.
Outcomes of percutaneous angioplasty interventions and/or stenting for below-the-knee PAD are available throughout the literature. Findings suggest that use of stents that elute anti-proliferative agents may result in further benefit in terms of restenosis rates as compared to uncoated PTA and bare metal stents.
Paclitaxel is an antineoplastic drug that has demonstrated sustained inhibition of smooth muscle cell proliferation in several pre-clinical studies.
Publications assessing effectiveness of local administration of paclitaxel on restenosis via drug-coated balloons in the femoropopliteal artery have shown promising results, as seen by reduced neointimal proliferation in the peripheral arteries. Recent publications have discussed outcomes regarding use of paclitaxel-coated balloons in patients with below-the-knee disease. Early studies using paclitaxel-coated balloons to manage complex below-the-knee lesions have shown paclitaxel-coated balloons to be superior to uncoated balloons with regard to restenosis rates. More recently, the results of a retrospective analysis of the Lutonix Paclitaxel coated balloon were published. Authors conclude that the Lutonix DCB showed safety and efficacy in BTK interventions in CLI patients.

Study objective

To assess the safety and efficacy of the paclitaxel drug-eluting balloon IN.PACT 014 versus conventional, optimal percutaneous transluminal angioplasty (PTA) for the treatment of patients with chronic total occlusions in the infrapopliteal arteries. This information can be used for regulatory purposes.

Study design

This is a prospective, multi-center, randomized (1:1) study to evaluate the efficacy and safety of the IN.PACT 014 in the treatment of CTOs in the infrapopliteal arteries.
All subjects will be followed with baseline, procedure, discharge, and follow-up evaluations at 30 days, 3, 6, 9, 12 and 24 months post procedure.

Intervention

The IN.PACT 014 is a medical device that contains an ancillary medicinal substance. The product consists of an over-the-wire (OTW) balloon catheter with a drug-coated balloon at the distal tip. The product is indicated for percutaneous transluminal angioplasty in patients with obstructive disease of peripheral arteries. The IN.PACT 014, including its components, is considered an investigational product.
The medicinal substance component, referred to as the Freepac* drug coating, consists of the medicinal substance paclitaxel and the excipient urea provides a nominal drug dose density of 3.5µg/mm2. The device component physically dilates the vessel lumen by Percutaneous Transluminal Angioplasty (PTA) (primary mode of action), and the medicinal substance provides a pharmacological agent targeted towards reducing the injury response that leads to restenosis (secondary mode of action).

Study burden and risks

Based on our current knowledge, participation into the IN.PACT BTK Clinical Study does not impose significant additional risks to the subject comparing to existing treatment option (ie. PTA, stenting). There is a high probability that subjects benefit when using a DCB as studies have shown clinical and angiographic superiority when compared to standard PTA in related treatment areas.
It is anticipated that the potential benefits of the study outweigh the potential risks; therefore the investigation is considered justified. It is possible in any clinical trial that unanticipated effects can happen which are not yet known at this time.

Contacts

Public
Medtronic B.V.

Endepolsdomein 5
Maastricht 6229 GW
NL
Scientific
Medtronic B.V.

Endepolsdomein 5
Maastricht 6229 GW
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Age >=18 years
2. Subject has been informed of the nature of the study, agrees to participate and has signed an Ethics Committee (EC) approved consent form.
3. Female subjects of childbearing potential have a negative pregnancy test <=7 days before the procedure and are willing to use a reliable method of birth control for the duration of study participation. Female subjects will be exempted from this requirement in case they are sterile, infertile, or have been post-menopausal for at least 12 months (no menses).
4. Subject has documented chronic Critical Limb Ischemia (CLI) in the target limb prior to the study procedure with Rutherford Clinical Category 4 or 5.
5. Subjects with documented infection grade 0-2 and ischemia grade 2-3 according to the WIfI classification.
6. Life expectancy >1 year in the Investigator*s opinion.
7. Reference Vessel Diameter (RVD) 2 - 4 mm, and confirmed by DUS assessment.
8. Total occlusions (100% stenosis) with total lesion length >=40mm (by visual estimate).
9. The lesion must be located in the infrapopliteal arteries and above the ankle joint. Lesions may not extend above the tibioperoneal trunk (P3 segment of the popliteal artery) or below the ankle joint (arteries of the foot), nor can the treatment (investigational device or standard PTA, including pre-dilatation) extend beyond these indicated regions for more than 1 cm.
Note:
• A target lesion can extend into the P3 segment in case it involves a straight lesion extending from the target vessel.
• Non-significant stenosis below the ankle joint can be allowed in case this is not part of the target lesion and does not require treatment
10. Multiple lesions can be treated if they are located in separate vessels but all lesions must meet the protocol specified criteria.
11. Presence of documented run-off to the foot (clearly visible dorsalis pedis, pedal arch or plantar arteries by angiography). Target vessel should give direct or indirect run-off to the foot

12. Inflow free from flow-limiting lesion confirmed by angiography. Patients with flow-limiting inflow lesions (>= 50% stenosis) can be included if lesion(s) have been treated successfully before enrollment, with a maximum residual stenosis of <=30% per visual assessment. If an inflow lesion must be treated within the P3 segment of the popliteal artery, there must be a minimum of 3 cm healthy tissue between this (treated) lesion and the infrapopliteal target lesion.
13. Successful pre-dilatation of the (entire) target lesion. Success being documented by angiographic visual estimate of <=30% Residual diameter stenosis of the target lesion and by functional assessment of the distal flow by intra-operative Doppler: recording of biphasic or triphasic wave signal with rapid take-off distal to the target lesion.

Exclusion criteria

1. Subject unwilling or unlikely to comply to the appropriate follow-up times for the duration of the study.
Note: the investigator should discuss the follow-up requirements extensively during the informed consent process to ensure that the subject is fully aware about the expectations and is willing to comply with the follow-up schedule.
2. Planned index limb amputation above the metatarsal level, or any other planned major surgery within 30 days pre or post-procedure. A planned amputation including and below the metatarsal level (1 or multiple rays) is accepted.
3. Lesion and / or occlusions located or extending in the popliteal artery or below the ankle joint space.
Note:
• A target lesion can extend into the P3 segment in case it involves a straight lesion extending from the target vessel
• Non-significant stenosis below the ankle joint can be allowed in case this is not part of the target lesion and does not require treatment.
4. Significant (>=50% DS) inflow lesion or occlusion in the ipsilateral Iliac, SFA and popliteal arteries left untreated.
5. Failure to obtain a <=30% residual stenosis in pre-existing, hemodynamically significant (>=50% DS) inflow lesions in the ipsilateral iliac, SFA and popliteal artery. Inflow lesions should be treated per standard of care.
6. Prior stent(s) or bypass surgery within the target vessel(s) (including stents placed within target vessels during the index procedure prior to randomization).
7. Previous DCB procedure in the target vessel within 6 months prior to index procedure.
8. Aneurysm in the target vessel.
9. Angiographic evidence of thrombus within target limb.
10. Pre-dilation resulted in a major (>= Grade D) flow-limiting dissection (observed on 2 orthogonal views) or residual stenosis >30%.
11. Use of alternative therapy, e.g. atherectomy, cutting balloon, laser, radiation therapy, stents as part of target vessel treatment. Note: Use of stents is only allowed for bailout stenting.
12. Recent MI or stroke <30 days prior to the index procedure.
13. Heart failure with Ejection Fraction <30%.

14. Known or suspected active infection at the time of the index procedure (abnormal white blood cell count, fever, sepsis or positive blood culture), excluding an infection of a lower extremity wound on the target limb (only WIfI infection grade 0-2 allowed).
15. Subjects with infection grade 3 and ischemia grade 0 and 1 according to WIfI classification.
16.Subjects with neurotrophic ulcers, heel pressure ulcers or calcaneal ulcers with a risk for major amputation.
17. Subjects with documented active osteomyelitis, excluding the phalanges, that is beyond cortical involvement of the bone per clinical judgement.
18. Impaired renal function (GFR <20 mL/min) or patients on dialysis.
19. Subject with vasculitis, systemic Lupus Erythematosus or Polymyalgia Rheumatica on active treatment.
20. Patient receiving systemic corticosteroid therapy (expected dosage exceeding 5mg of prednisolone or equivalent, per day during the initial 9 months after procedure).
21. This criteria has been removed
22. Known allergies or sensitivities to heparin, aspirin (ASA), other anticoagulant/anti-platelet therapies which could not be substituted, and/or paclitaxel or an allergy to contrast media that cannot be adequately pre-treated prior to the index procedure.
23. The patient is currently enrolled in another investigational device or drug trial that is interfering with the endpoints of this study.
24. Female subjects who are breast-feeding at the time of enrollment

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	8
Type:	Anticipated

Medical products/devices used

Generic name:	Paclitaxel-Coated Percutaneous Transluminal Angioplasty Balloon Catheter
Registration:	No

Ethics review

Approved WMO Date:	09-11-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-02-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-12-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
ClinicalTrials.gov	NCT02963649
CCMO	NL62158.091.17