T.I.N.T.I.N. STUDY

PROTOCOL SYNOPSIS

V2.0- 20200323

Title	T.I.N.T.I.N.: Physician initiated, prospective, non-randomized Belgian multi-center trial, Investigating the safety and efficacy of the **T**reatment with the Lum**IN**or DCB and **T**he **I**volutio**N** stent of iVascular in TASC C and D femoropopliteal atherosclerotic disease
Objective	The objective of this clinical investigation is to evaluate the long-term (up to 5 years)outcome of the combination therapy with the Luminor DCB and the iVolution stent of iVascular for the treatment of long femoropopliteal lesions (TASC C & D)
Methodology	Prospective, multi-center, physician initiated clinical study
Enrollment	100 subjects
Primary Endpoint	*Efficacy endpoint*: Freedom from clinically-driven TLR at 12 months: TLR defined as a repeated intervention to maintain or re-establish patency within the region of the treated arterial vessel plus 5mm proximal and distal to the treated lesion edge at the respective time points
Secondary Endpoints	1. Primary patency rate at 6- and 12-month follow-up; defined as absence of a hemodynamically significant stenosis on duplex ultrasound (systolic velocity ratio no greater than 2.5) at the target lesion and without TLR within the time of procedure and the given follow-up. 2. Technical success; defined as the ability to cross and dilate the lesion and achieve residual angiographic stenosis no greater than 30% 3. Freedom from clinically-driven TLR at 6-month, 2, 3, 4 and 5 year follow-up; TLR defined as a repeated intervention to maintain or re-establish patency within the region of the treated arterial vessel plus 5mm proximal and distal to the treated lesion edge at the respective time points 4. Clinical success at follow-up; defined as an improvement of Rutherford classification at all follow-up time points of one class or more as compared to the pre-procedure Rutherford classification 5. Serious adverse events as defined per ISO 14155:2011
Inclusion Criteria	1. Patient presenting a score from 2 to 5 following Rutherford classification 2. Patient is willing to comply with specified follow-up evaluations at the specified times 3. Patient is >18 years old 4. Patient understands the nature of the procedure and provides written informed consent, prior to enrolment in the study 5. Patient has a projected life expectancy of at least 12 months 6. Prior to enrolment, the guidewire has crossed target lesion

7. Patient is eligible for treatment with the Luminor Paclitaxel-Eluting Peripheral Balloon Dilatation Catheter and the iVolution stent
8. Male, infertile female or female of child bearing potential practicing an acceptable method of birth control with a negative pregnancy test within 7 days prior to study procedure

Angiographic Inclusion Criteria

1. De novo and post-PTA restenotic lesions located in the femoropopliteal arteries suitable for endovascular therapy
2. The target lesion is located within the native femoropopliteal artery
3. The length of the target lesion is ≥ 150mm and considered as TASC C or D lesion according to the TASC II classification.
4. The target lesion has angiographic evidence of stenosis > 50% or occlusion which can be passed with standard guidewire manipulation
5. Target vessel diameter visually estimated is >4mm and <6.5 mm
6. There is angiographic evidence of at least one-vessel-runoff to the foot, irrespective of whether or not outflow was re-established by means of previous endovascular intervention

Exclusion Criteria

1. Patient refusing treatment
2. Presence of a stent in the target lesion that was placed during a previous procedure
3. Untreated flow-limiting inflow lesions
4. Any previous surgery in the target vessel (including prior ipsilateral crural bypass)
5. Patients for whom antiplatelet therapy, anticoagulants or thrombolytic drugs are contraindicated
6. Patients who exhibit persistent acute intraluminal thrombus of the proposed lesion site
7. Perforation at the angioplasty site evidenced by extravasation of contrast medium
8. Patients with known hypersensitivity to heparin, including those patients who have had a previous incidence of heparin-induced thrombocytopenia (HIT) type II
9. Patients with uncorrected bleeding disorders
10. Aneurysm located at the level of the SFA/popliteal artery
11. Non-atherosclerotic disease resulting in occlusion (e.g. embolism, Buerger's disease, vasculitis)
12. Severe medical comorbidities (untreated CAD/CHF, sever COPD, metastatic malignancy, dementia, etc.) or other medical condition that would preclude compliance with the study protocol or 1-year life expectancy
13. Major distal amputation (above the transmetatarsal) in the study limb or non-study limb
14. Septicemia or bacteremia
15. Use of thrombectomy, atherectomy or laser devices during procedure
16. Any patient considered to be hemodynamically unstable at onset of procedure
17. Known allergy to contrast media that cannot be adequately pre-medicated prior to the study procedure

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Study conduct

The study will be conducted in accordance with the Declaration of Helsinki and ISO 14155:2011, and comply with requirements regarding Ethics Committees and any other applicable regulations.

Study investigations

Time	Tests and Procedures
Pre-Procedure (up to 24 hours before procedure, unless otherwise noted)	1. Medical History 2. Medication Registration 3. Physical Exam (ABI, Rutherford) 4. Consenting patient
Procedure	1. Angiography, pre–procedure 2. Study inclusion 3. Intervention details 4. Angio post-procedure 5. Adverse Event recording/reporting
1 day Post-Procedure	1. Medication Registration 2. Physical Examination (ABI, Rutherford) 3. Adverse Event recording/reporting
1 month Follow-up (± 7 days)	1. Medication Registration 2. Physical Examination (ABI, Rutherford) 3. Color Flow Doppler Ultrasound 4. Adverse Event recording/reporting
6 month Follow-up (± 30 days)	1. Medication Registration 2. Physical Examination (ABI, Rutherford) 3. Color Flow Doppler Ultrasound 4. Adverse Event recording/reporting
12 month Follow-up (± 30 days)	1. Medication Registration 2. Physical Examination (ABI, Rutherford) 3. Color Flow Doppler Ultrasound 4. Adverse Event recording/reporting
2 year Follow-up (± 30 days)	1. Medication Registration 2. Physical Examination (ABI, Rutherford) 3. Adverse Event recording/reporting
3 year Follow-up (± 30 days)	1. Medication Registration 2. Physical Examination (ABI, Rutherford) 3. Adverse Event recording/reporting
4 year Follow-up (± 30 days)	1. Medication Registration 2. Physical Examination (ABI, Rutherford)Adverse Event 3. recording/reporting
5 year Follow-up (± 30 days)	1. Medication Registration 2. Physical Examination (ABI, Rutherford) 3. Adverse Event recording/reporting

Participating sites

- Dr Deloose, AZ Sint-Blasius, Dendermonde, Belgium
- Dr Maene, OLV-ziekenhuis, Aalst, Belgium
- Dr. Keirse, RZ Tienen, Tienen, Belgium
- Dr Goverde, ZNA Stuivenberg, Antwerp, Belgium
- Dr. Verbist, Imelda, Bonheiden, Belgium
- Dr. Schepers, AZ Damiaan, Oostende, Belgium
- Dr. Dubois, Heilig Hartziekenhuis, Lier, Belgium
- Dr. Balduyk, Sint Jozefkliniek, Bornem, Belgium
- Dr. Robijn, AZ Jan Portaels ziekenhuis, Vilvoorde, Belgium

Statistical Analysis Plan (SAP)

Descriptive data summaries will be used to present and summarize the collected data. For categorical variables (e.g. Gender) frequency distributions and cross tabulations will be given. For numeric variables (e.g. Patient age) minimum, maximum, mean, median and standard deviation will be calculated. For all variables a 95% confidence interval for the relevant parameters of the underlying distribution will be calculated. For all time-dependent events life-tables will be calculated using the Kaplan Meier estimate method, for a period starting on the date of the procedure up to and including the 12-month follow-up visit. Stratification to pre-procedural risk factors, Rutherford and lesion criteria will be performed and the log rank test will be used to compare between the different outcomes, associated p-values < 0.05 are defined as significant.