Clinical Design of the FIRST and ONLY Approved IDE BTK Trial for a Drug Coated Balloon

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- The presenter is a consultant of Lutonix, Inc. and Bard Peripheral Vascular, Inc.
- The opinions and clinical experiences presented herein are for informational purposes only. The results presented may not be predictive for all studies and patients. Results may vary depending on a variety of experimental and clinical parameters.
Conflicts of Interest
# Trial Summary

## PRIMARY ENDPOINTS
- Safety at 30 days
- Limb salvage & primary patency at 12 months

## NUMBER OF PATIENTS/SITES
- 320 randomized patients at 55 global sites

## FOLLOW-UP
- **Clinical:** 1, 6, 12, 24, and 36 Months
- **Duplex Ultrasound (DUS):** 1, 6,12, 24, & 36 months
- **Angiography:** 12 months
- **Telephone:** 48 and 60 Months

## NATIONAL PRINCIPAL INVESTIGATORS
- **Patrick Geraghty:** Washington University, St. Louis, MO
- **Jihad Mustapha:** Metro Health Hospital, Wyoming, MI
- **Marianne Brodmann:** Medical University Graz, Austria

## SPONSOR
- Lutonix Inc., Minneapolis, MN

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Primary Endpoints

SAFETY
Freedom from Major Adverse Limb Events & All-Cause Death at 30 DAYS

- Amputation (above ankle)
- Major re-intervention
  - New bypass graft
  - Jump/Interposition graft revision
  - Thrombectomy/Thrombolysis

EFFICACY
Composite of Limb Salvage and Primary Patency at 12 Months

Defined as freedom from the composite of above ankle amputation, target vessel occlusion, and clinically-driven target lesion re-intervention.

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## Inclusion Criteria

- Male or non-pregnant female ≥18 years of age
- Rutherford 4-5
- Life expectancy ≥ 1 year
- Significant stenosis (≥70%)
- A patent inflow artery
- Target vessel(s) diameter between 2 and 4 mm
- Target vessel(s) reconstitute(s) at or above the ankle

## Exclusion Criteria

- Pregnant or planning on becoming pregnant
- History of stroke within 3 months
- History of MI, thrombolysis or angina within 30 days of enrollment
- Prior or planned major amputation
- GFR ≤ 30 ml/min per 1.73m$^2$
- Acute limb ischemia
- In-stent restenosis of target lesion

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Protocol Features

- Randomized 2:1 versus POBA
- Permits treatment of two tibial arteries (two flow pathways)
- Combined lesion length of up to 32 cm treatable (36 cm balloon length allowed)
- Retrograde wire access permitted, but not retrograde intervention
- Balloon lengths of up to 12 cm
- First U.S. use of tibial patency assessment via duplex ultrasound (VasCore)
- Angiographic assessment of normal-risk subset at one year (Synvacor)
- Broad range of secondary endpoints including QOL instruments

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Inflow Treatment

If needed

PTA Pre-Dilatation
With Uncoated Balloon

Successful PTA with Outflow

Randomize 2:1

Test Arm:
Dilatation of ALL target lesions with Drug Coated Balloon

Control Arm:
Dilatation of ALL target lesions with Uncoated Balloon

Suboptimal PTA
Absence of above ankle reconstitution
>75% residual stenosis

Treat per standard practice
30 day follow-up for safety

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What is the Data Monitoring Committee?

- Unbiased panel of leading experts in peripheral vascular disease, cardiovascular medicine and biostatistics not associated with Lutonix or the trial

- During the enrollment phase of the trial, DMC reviews accumulating safety data to monitor for incidence of serious vascular events that would warrant termination of the trial
Safety Review

5 Data Monitoring Committee meetings to date

165 randomized patients:
- 95 have completed 6 month follow-up
- 39 have completed 12 month follow-up

Only 5 major amputations (3% of enrolled pts) recorded

This is the Only approved and ongoing BTK trial in the US

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INDICATIONS FOR USE: The LUTONIX® 035 Drug Coated Balloon PTA catheter is indicated for percutaneous transluminal angioplasty, after pre-dilatation, of de novo or restenotic lesions up to 150mm in length in native superficial femoral or popliteal arteries with reference vessel diameters of 4-6mm.

CONTRAINDICATIONS : The LUTONIX® Catheter is contraindicated for use in: 1) Patients who cannot receive recommended anti-platelet and/or anticoagulant therapy. 2) Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and there is a potential for adverse reaction in nursing infants from paclitaxel exposure. 3) Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.

WARNINGS: Contents supplied STERILE using ethylene oxide (EO) process. Do not use if sterile barrier is damaged or opened prior to intended use. Do not use if product damage is evident. The LUTONIX® Catheter is for use in one patient only; do not reuse in another patient, reprocess or resterilize. Risks of reuse in another patient, reprocessing, or resterilization include: Compromising the structural integrity of the device and/or device failure which, in turn, may result in patient injury, illness or death. Creating a risk of device contamination and/or patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to patient injury, illness or death. Do not exceed the Rated Burst Pressure (RBP) recommended for this device. Balloon rupture may occur if the RBP rating is exceeded. To prevent over-pressurization, use of a pressure monitoring device is recommended. Use the recommended balloon inflation medium of contrast and sterile saline (≤50% contrast). Never use air or any gaseous medium to inflate the balloon. This product should not be used in patients with known hypersensitivity to paclitaxel or structurally related compounds. The safety and effectiveness of the Lutonix® Catheter have not been established for treatment in cerebral, carotid, coronary, or renal vasculature. The safety and effectiveness of using more than two Lutonix drug coated balloons (i.e., a maximum drug coating quantity of approximately 7.6 mg paclitaxel) in a patient has not been clinically evaluated.

PRECAUTIONS : General Precautions: The LUTONIX® Catheter should only be used by physicians trained in percutaneous interventional procedures. Consideration should be given to the risks and benefits of use in patients with a history of non-controllable allergies to contrast agents.

POTENTIAL ADVERSE EVENTS: Potential adverse events which may be associated with a peripheral balloon dilatation procedure include: Additional intervention, allergic reaction to drugs, excipients or contrast medium, amputation/loss of limb, aneurysm or pseudoaneurysm, arrhythmias, embolization; hematoma; hemorrhage, including bleeding at the puncture site, hypotension/hypertension, inflammation, occlusion, pain or tenderness, pneumothorax or hemothorax, sepsis/infection, shock, stroke, thrombosis, vessel dissection, perforation, rupture, or spasm. Although systemic effects are not anticipated, refer to the Physicians’ Desk Reference for more information on the potential adverse events observed with paclitaxel. Potential adverse events, not described in the above source, which may be unique to the paclitaxel drug coating include: Allergic/immunologic reaction to the drug coating (paclitaxel), alopecia, anemia, blood product transfusion, gastrointestinal symptoms, hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia), hepatic enzyme changes, histologic changes in vessel wall, including inflammation, cellular damage, or necrosis, myalgia/arthritis, myelosuppression and peripheral neuropathy.

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