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# LUTONIX<sup>®</sup> DCB in BTK – Update on the BTK clinical program & single center experience

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# Disclaimer

- This presentation is on behalf of Lutonix, Inc., a subsidiary of C.R. Bard, Inc. It is intended as an update and exchange of scientific and clinical trial information.
- 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.

# Disclosures

Speaker's name: Sabine Steiner

I have the following potential conflicts of interest to report:

Consulting:

Abbott, C.R. Bard

# How to Improve Patency BTK

- Drug-eluting stents (short, focal lesion)
- Local Drug-delivery without stenting
  - ✗ Drug-coated balloons
  - ✗ Micro-Infusion Device: Bullfrog<sup>®</sup>

# Drug-Coated Balloon BTK

Trials which failed to show a benefit / superiority for DCBs BTK

- In.Pact DEEP multicentric, randomized, controlled trial
  - In.Pact Amphirion PTX-eluting balloon vs.
  - Uncoated Amphirion Deep

Zeller et al. *JACC* 2014

- ✗ Biolux-P-II multicentric, randomized, controlled trial
  - ✓ Passeo-18 LUX PTX-eluting balloon vs.
  - ✓ Uncoated Passeo-18

Zeller et al. *JACC Intervent* 2015

# German single center experience with Lutonix<sup>®</sup> DCB in infrapopliteal arteries

- Retrospective cohort study of patients undergoing below-the-knee interventions using Lutonix<sup>®</sup> drug coated balloons
- 248 patients treated, 40 lost to follow-up (16%)
- 220 limbs treated in 208 patients with CLI or claudication

# Study design

- Clinical follow up
  - Rate of death
  - BTK target lesion revascularization and re-interventions
  - Minor and major amputations
  - Ulcer healing
  - Improvement of Rutherford classification

# Baseline patient characteristics

Variable	BTK Cohort (n= 208)
Age (years), mean $\pm$ std	74.1 $\pm$ 9.7
Male, n (%)	138 (66.4%)
Hyperlipidemia, n (%)	160 (77%)
Diabetes mellitus, n (%)	144 (69%)
Arterial Hypertension, n (%)	198 (95%)
Current smoking, n (%)	54 (26%)
Former smoking, n (%)	40 (19%)
Coronary heart disease, n (%)	98 (47%)
Cerebrovascular disease, n (%)	17 (8%)



# Rutherford classification

Rutherford category prior to intervention, n (%)	
Stage 3	85 (38.7%)
Stage 4	27 (12.3%)
Stage 5	102 (46.4%)
Stage 6	6 (2.7%)

# Lesion characteristics

	N=220
<b>Lesion characteristics</b>	
Treatment of total occlusion, n (%)	140 (63.6%)
No. of open BTK vessels before intervention, n (%)	
0	37 (16.8%)
1	106 (48.2%)
2	66 (30.0%)
3	11 (5%)
BTK vessel treated with DCB*	
Tibioperoneal trunk, n (%)	44 (20.0%)
Posterior tibial artery, n (%)	55 (25.0%)
Peroneal artery, n (%)	57 (25.9%)
Anterior tibial artery, n (%)	118 (53.6%)

\*Several arteries could be treated during one intervention

# Procedural characteristics

	N=220
<b>Procedural characteristics and outcomes</b>	
No. of devices used, mean± std	2.3±1.1
Cumulative length of devices (mm), mean± std	242.5±125.1
Mean diameter of devices (mm), mean± std	2.7±0.3
BTK stent implantation, n (%)	38 (17.3%)
Special balloons for lesion preparation, n (%)	4 (1.8%)
Treatment of inflow lesions, n (%)	105 (48%)
Femoropopliteal, n (%)	63 (29%)
Popliteal, n (%)	42 (19%)
Treatment of pedal arch, n (%)	19 (8.6%)
Retrograde recanalization, n (%)	27 (12.3%)
Relevant residual stenosis (>30%)*, n (%)	2 (0.9%)

\*Lack of restoration of at least one BTK artery with > 30% residual stenosis

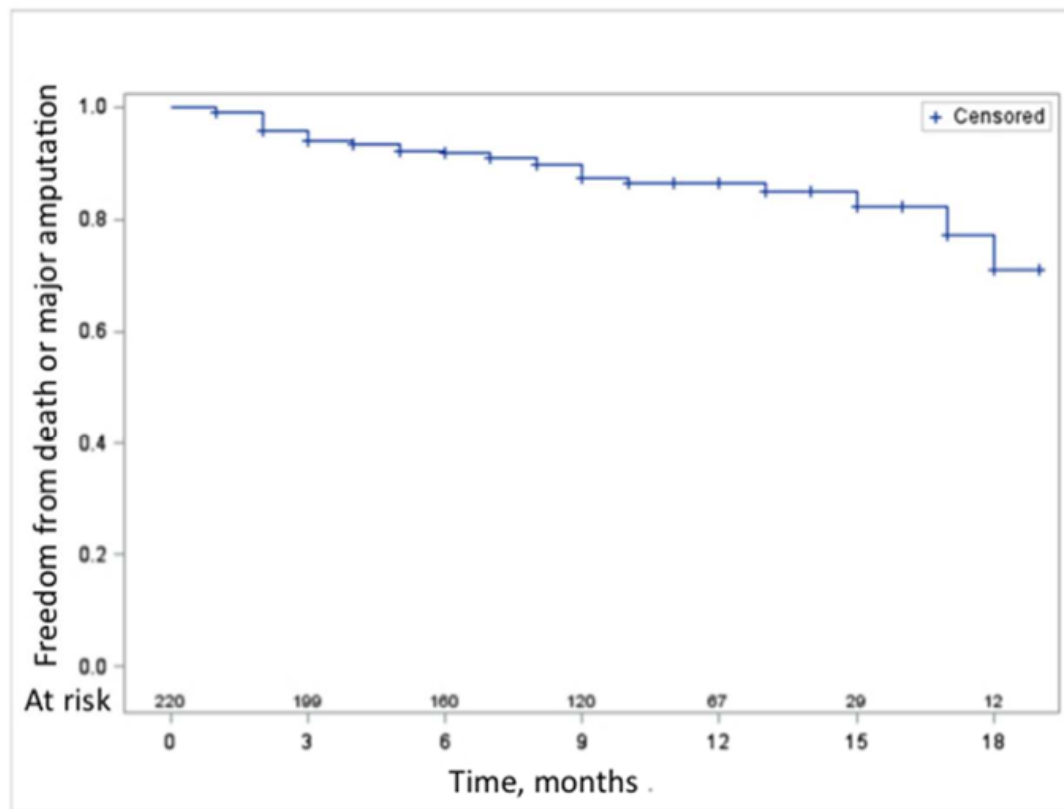
# Follow up I - Death

- Median follow up time was 9 months (range 1-19 months)
- 75% had a follow up time  $\geq$  6 months
- 22 (10.6%) patients died during follow up
  - 7 for cardiac reasons
  - 1 due to stroke
  - 1 due pulmonary embolism
  - 1 due to septicemia after major amputation (2mo after intervention)
  - 12 deaths outside hospital for unclear reasons

# Follow up

<b>Variable</b>	<b>Full cohort (208 pts; 220 limbs)</b>	<b>Claudicants (80 pts; 85 limbs)</b>	<b>CLI (128 pts; 135 limbs)</b>
All-cause mortality	22 (10.6%)	3 (3.8%)	19 (14.8%)
Major amputations	9 (4.1%)	-	9 (6.7%)

# Freedom from death/major amputation



Time, months	0	3	6	9	12	15	18
Survival %	100	93.9	91.8	87.5	86.6	82.2	70.9
Std. Error	0	1.6	1.9	2.5	2.6	4.1	8.2

# Follow up

Variable	Full cohort (208 pts; 220 limbs)	Claudicants (80 pts; 85 limbs)	CLI (128 pts; 135 limbs)
All-cause mortality	22 (10.6%)	3 (3.8%)	19 (14.8%)
Major amputations	9 (4.1%)	-	9 (6.7%)
BTK re-intervention*	50 (22.7%)	17 (20%)	33 (24.4%)
Target lesion revascularization	35 (15.9%)	11 (12.9%)	24 (17.8%)

\*Including pre-planned secondary interventions

# Follow up

Variable	Full cohort (208 pts; 220 limbs)	Claudicants (80 pts; 85 limbs)	CLI (128 pts; 135 limbs)
All-cause mortality	22 (10.6%)	3 (3.8%)	19 (14.8%)
Major amputations	9 (4.1%)	-	9 (6.7%)
BTK re-intervention*	50 (22.7%)	17 (20%)	33 (24.4%)
Target lesion revascularization	35 (15.9%)	11 (12.9%)	24 (17.8%)
Improvement of $\geq 1$ Rutherford category	130 (59.1%)	46 (54.1%)	84 (62.2%)
Wound healing*	-	-	68 (76.4%)

\*Outcome data on wound healing was available for 82.4% of patients (n=89) with baseline Rutherford category 5 and 6



# Summary

- Real world data of patients undergoing below the knee interventions using Lutonix<sup>®</sup> DCB
- Clinical follow-up suggests re-assuring effectiveness and safety profile

# LUTONIX

## BTK Clinical Trial



# Trial Summary

<b>PRIMARY ENDPOINTS</b>	Safety at 30 days Limb salvage & primary patency at 12 months
<b>NUMBER OF PATIENTS/SITES</b>	320 randomized patients at 55 global sites
<b>FOLLOW-UP</b>	<b>Clinical:</b> 1, 6, 12, 24, and 36 Months <b>Duplex Ultrasound (DUS):</b> 1, 6, 12, 24, & 36 months <b>Angiography :</b> 12 months <b>Telephone:</b> 48 and 60 Months
<b>NATIONAL PRINCIPAL INVESTIGATORS</b>	<b>Patrick Geraghty:</b> Washington University, St. Louis, MO <b>Jihad Mustapha:</b> Metro Health Hospital, Wyoming, MI <b>Marianne Brodmann:</b> Medical University Graz, Austria
<b>SPONSOR</b>	Lutonix Inc., Minneapolis, MN

Caution – Investigational Device, Limited by Federal (USA) Law to Investigational Use



# 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.





# Patient Eligibility

## Inclusion Criteria

- Male or non-pregnant female  $\geq 18$  years of age
- Rutherford 4-5
- Life expectancy  $\geq 1$  year
- Significant stenosis ( $\geq 70\%$ )
- 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
- $\text{GFR} \leq 30$  ml/min per  $1.73\text{m}^2$
- Acute limb ischemia
- In-stent restenosis of target lesion



## 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

# Study Flowchart

**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



# Safety Review

- 8 Data Monitoring Committee meetings so far
- 273 randomized patients:
  - 184 have completed 6 month follow-up
  - 134 have completed 12 month follow-up
- Only 11 major amputations (3% of enrolled pts) recorded
- **Only approved and ongoing BTK trial in the US**

## **INTENDED USE / INDICATIONS FOR USE**

The Lutonix® 035 Drug Coated Balloon Catheter is intended for use as a PTA catheter to dilate stenotic or obstructive vascular lesions in the lower extremities, and native or synthetic arteriovenous fistula, for the purpose of improving limb perfusion, and decreasing the incidence of restenosis

## **CONTRAINDICATIONS**

The Lutonix® Catheter is contraindicated for use in:

- Patients who cannot receive recommended anti-platelet and/or anticoagulant therapy.
- 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.
- Pediatric patients. The safety and effectiveness of the Lutonix® Catheter in pediatric patients has not been established.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.
- This product should not be used in patients with known hypersensitivity to paclitaxel or structurally related compounds.

## **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.
- The safety and effectiveness of the Lutonix® Catheter have not been established for treatment in cerebral, carotid, coronary, or renal vasculature.
- Based on safety studies in animals, cumulative paclitaxel dose should not exceed 21.5mg. For example, using Table 1 (above), a total of 3 balloons would provide a cumulative dose of 17.1mg for a 6mm x 150mm balloon.

## **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
- 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

Potential adverse events that may be unique to the Lutonix® Catheter paclitaxel drug coating:

- Allergic reaction to drug coating

There may be other potential adverse events that are unforeseen at this time.



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