**LUTONIX® BTK Trial**

A Prospective, Multicenter, Single Blind, Randomized, Controlled Trial Comparing the Lutonix Drug Coated Balloon vs. Standard Balloon Angioplasty for Treatment of Below-the-Knee (BTK) Arteries

Patrick Geraghty, MD, FACS
Professor of Surgery and Radiology
Co-Director, Limb Salvage Center

**CLI Impact**

1 year after primary treatment for CLI

- Approximately 120,000 amputations are performed annually.
- The estimated lifetime direct healthcare cost for an amputee patient is $794,027.
- When aggregated for the total number of lower extremity amputation patients annually, the expected lifetime cost is estimated at roughly $96.2 billion USD.

**Study Co-Principal Investigators**

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- Dr. Jihad Mustapha
  Advanced Cardiac & Vascular Amputation Prevention Centers
  1525 East Beltline NE, Suite 101
  Grand Rapids, MI 49525

**LUTONIX® Global Below-the-Knee Study**

Enrollment by Geography

- US: 275
- EU: 122
- Japan: 40
- Canada: 5

442 Randomized Subjects (DCB - 287, PTA - 155)

Multicenter participation: 51 sites

8 countries

Enrollment: Jun 2013 – Dec 2017

**Study Centers**

Pending PMA, not available for sale within the United States.
Study Synopsis

Objective
To demonstrate the superior efficacy and non-inferior safety of the Lutonix DCB by direct comparison to standard PTA for treatment of stenoses or occlusion of below-the-knee arteries

Study Design
Prospective, Multi-center, Single Blind, Randomized, Safety and Efficacy

Test Device
LUTONIX® 0.014” OTW Drug Coated PTA Dilatation Catheter

Randomization
Subjects will be randomized 2:1 to Lutonix DCB or standard PTA catheter.

Clinical Follow-up
1, 6, 12, 24, 36 Months

Primary Endpoints

SAFETY
Freedom from Major Adverse Limb Events (MALE) & All-Cause Perioperative Death (POD) 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 6 Months
* Defined as freedom from a composite of above ankle amputation, target vessel occlusion, and clinically-driven target lesion revascularization

Patient Eligibility

Inclusion Criteria
✓ Male or non-pregnant female ≥18 years of age
✓ Rutherford 3-5
✓ 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
✓ History of stroke within 3 months
✓ History of MI, thrombolysis or angina within 30 days of enrollment
✓ GFR ≤ 30 ml/min per 1.73m²
✓ Acute limb ischemia
✓ In-stent restenosis of target lesion

Demographics and Risk Factors

<table>
<thead>
<tr>
<th></th>
<th>DCB N=287</th>
<th>PTA N=155</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Mean ± SD (n)</td>
<td>72.9 ± 9.65 (287)</td>
<td>72.9 ± 9.62 (155)</td>
<td>0.5086</td>
</tr>
<tr>
<td>Gender, % (n/N)</td>
<td>Male 70.4% (202/287)</td>
<td>Female 29.6% (85/287)</td>
<td>0.5173</td>
</tr>
<tr>
<td>Race, % (n/N)</td>
<td>American Indian or Alaska Native 0.3% (1/287)</td>
<td>Asian 8.7% (25/287)</td>
<td>0.7468</td>
</tr>
<tr>
<td></td>
<td>Black or African American 11.5% (33/287)</td>
<td>White 78.7% (226/287)</td>
<td>0.0036</td>
</tr>
<tr>
<td></td>
<td>Other 0.7% (2/287)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Demographics and Risk Factors

<table>
<thead>
<tr>
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<th>DCB N=287</th>
<th>PTA N=155</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of Risk Factors, % (n/N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>96.3% (276/287)</td>
<td>96.4% (151/155)</td>
<td>0.9346</td>
</tr>
<tr>
<td>Cigarette Smoking</td>
<td>76.4% (223/287)</td>
<td>74.8% (116/155)</td>
<td>0.4210</td>
</tr>
<tr>
<td>Hypertension</td>
<td>92.6% (268/287)</td>
<td>91.8% (146/155)</td>
<td>0.3740</td>
</tr>
<tr>
<td>Other</td>
<td>85.9% (121/140)</td>
<td>90.9% (136/150)</td>
<td>0.3740</td>
</tr>
</tbody>
</table>

Subject has Undergone Any Previous Cardio Vascular Interventions
72.8% (209/287) 74.8% (116/155) 0.735

Subject has Undergone Previous Peripheral Vascular Interventions
53.7% (154/287) 54.2% (84/155) 0.921
Baseline Rutherford Category

DCB (N=287)
- Class 3: 34.8%
- Class 4: 56.1%
- Class 5: 9.1%

PTA (N=155)
- Class 3: 33.5%
- Class 4: 56.1%
- Class 5: 10.3%

P-Value 0.9181

Lesion Characteristics

DCB (N=351)
- TASC A: 51.9%
- TASC B: 17.4%
- TASC C: 17.7%
- TASC D: 13.1%

PTA (N=209)
- TASC A: 62.7%
- TASC B: 15.3%
- TASC C: 12.4%
- TASC D: 6.8%

P-Value 0.073

Preliminary Baseline Angio Data

<table>
<thead>
<tr>
<th>Number of Lesions by Vessel, % (n/N)</th>
<th>Treated Lesions DCB</th>
<th>Treated Lesions PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65.4% (275/422)</td>
<td>78.2% (140/181)</td>
</tr>
<tr>
<td>2</td>
<td>12.1% (50/422)</td>
<td>18.8% (41/221)</td>
</tr>
<tr>
<td>3</td>
<td>2.2% (9/422)</td>
<td>2.2% (4/181)</td>
</tr>
<tr>
<td>6</td>
<td>3.3% (13/422)</td>
<td>3.3% (5/181)</td>
</tr>
<tr>
<td>Mean Target Lesion Length, mm (n/N)</td>
<td>111.9 ± 92.6 mm (349/352)</td>
<td>94.7 ± 85.4 mm (206/213)</td>
</tr>
<tr>
<td>Mean Initial % Stenosis, % (n/N)</td>
<td>86.7 ± 14.0% (352/352)</td>
<td>84.6 ± 14.0% (212/213)</td>
</tr>
</tbody>
</table>

Preliminary Baseline Angio Data (Cont.)

<table>
<thead>
<tr>
<th>Vessel Locations, % (n/N)</th>
<th>Treated Lesions DCB</th>
<th>Treated Lesions PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Popliteal</td>
<td>10.2% (33/322)</td>
<td>9.3% (17/183)</td>
</tr>
<tr>
<td>Tibioperone Trunk</td>
<td>28.0% (90/322)</td>
<td>31.1% (57/183)</td>
</tr>
<tr>
<td>Anterior Tibial</td>
<td>41.0% (132/322)</td>
<td>35.5% (85/183)</td>
</tr>
<tr>
<td>Peroneal</td>
<td>24.2% (78/322)</td>
<td>27.3% (50/183)</td>
</tr>
<tr>
<td>Posterior Tibial</td>
<td>23.6% (76/322)</td>
<td>24.6% (45/183)</td>
</tr>
</tbody>
</table>

Primary Endpoints (30-Day Safety*)

<table>
<thead>
<tr>
<th></th>
<th>DCB (N=287)</th>
<th>PTA (N=155)</th>
<th>Difference in Response % (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free from Primary Safety Event at 30 Days</td>
<td>99.3% (283/285)</td>
<td>99.4% (154/155)</td>
<td>-0.1% (-3.9%, 3.8%)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

*Freedom at 30 days from TVR, major index limb amputation, and device and all cause death.
Primary Endpoints (6 Month Efficacy*)

<table>
<thead>
<tr>
<th></th>
<th>DCB</th>
<th>PTA</th>
<th>Difference in Response (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free from Primary Efficacy Failure at 6 Months</td>
<td>73.7% (196/266)</td>
<td>63.5% (87/137)</td>
<td>10.2% (-0.2%, 18.7%)</td>
<td>0.0273</td>
</tr>
</tbody>
</table>

*Freedom at 6 months from major index limb amputation, target lesion occlusion and CD-TLR.

Primary Endpoints by Gender

<table>
<thead>
<tr>
<th></th>
<th>DCB</th>
<th>PTA</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Safety</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender, % (n/N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>99.0% (983/993)</td>
<td>100.0% (988/988)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Female</td>
<td>99.3% (223/226)</td>
<td>99.6% (204/205)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pooled</td>
<td>99.0% (104/104)</td>
<td>99.0% (104/104)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Primary Efficacy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender, % (n/N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>73.1% (140/191)</td>
<td>62.1% (59/95)</td>
<td>14.0% (-0.2%, 18.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>74.7% (56/75)</td>
<td>66.7% (20/24)</td>
<td>8.0% (-1.7%, 6.4%)</td>
</tr>
<tr>
<td>Pooled</td>
<td>73.7% (196/266)</td>
<td>63.5% (87/137)</td>
<td>14.0% (-0.2%, 18.7%)</td>
</tr>
</tbody>
</table>

Secondary Endpoint

(KM 6 Month Primary Patency – Total Occlusion / CD-TLR)

<table>
<thead>
<tr>
<th></th>
<th>DCB</th>
<th>PTA</th>
<th>Difference in Response (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>88.3% DCB</td>
<td>72.3% PTA</td>
<td></td>
<td>14.0% (-0.2%, 18.7%)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Primary Endpoints (KM 30-Day Safety)

Primary Endpoints (KM 6 Month Efficacy)

Toe Brachial Index (Through 6 Months)
**Conclusion**

- **Primary safety endpoint met - no difference between DCB and PTA** (p=<0.0001*) at 30 days
- By Kaplan Meier estimate at 6 months: no difference in primary safety (DCB - 97.8% / PTA - 95.3%, p=0.096)
- Primary efficacy endpoint at 6 months: DCB - 73.7% / PTA - 63.5% (Δ10.2%, p=0.0273)
- By Kaplan Meier estimate at 6 month: primary efficacy DCB - 85.3% / PTA - 70.7% (Δ14.6%, p=<0.001*)

**Conclusion (Cont.)**

- Sustained hemodynamic improvement through 6 Months
- No gender differences - Primary Safety and Primary Efficacy
- By Kaplan Meier estimate at 6 month: Primary Patency DCB - 86.3% / PTA - 72.2% (Δ14.0%, p=<0.001*)
- By Kaplan Meier estimate at 6 month: TLR Free DCB - 93.8% / PTA - 85.5% (Δ8.3 %, p=<0.004*)
- Reduction in the presence of any wound at 6 months compared to enrollment; no difference between DCB and PTA

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**Secondary Endpoint (KM 6 Month CD-TLR Free)**

![Graph showing Kaplan-Meier estimates for DCB and PTA](image-url)

- 93.9% DCB
- 85.5% PTA
- 8.3% Δ (p <0.004)

**Wound Assessment**

<table>
<thead>
<tr>
<th></th>
<th>DCB Baseline</th>
<th>DCB 6 Months</th>
<th>PTA Baseline</th>
<th>PTA 6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Wound Present, %</td>
<td>59.2%</td>
<td>45.4%</td>
<td>58.0%</td>
<td>45.4%</td>
</tr>
<tr>
<td>n/N*</td>
<td>181/272</td>
<td>179/228</td>
<td>144/150</td>
<td>169/179</td>
</tr>
</tbody>
</table>

*Site reported, Non-standardized, Non-adjudicated

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**Conclusion**

- Primary safety endpoint met - no difference between DCB and PTA (p=<0.0001*) at 30 days
- By Kaplan Meier estimate at 6 months: no difference in primary safety (DCB - 97.8% / PTA - 95.3%, p=0.096)
- Primary efficacy endpoint at 6 months: DCB - 73.7% / PTA - 63.5% (Δ10.2%, p=0.0273)
- By Kaplan Meier estimate at 6 month: primary efficacy DCB - 85.3% / PTA - 70.7% (Δ14.6%, p=<0.001*)

**Conclusion (Cont.)**

- Sustained hemodynamic improvement through 6 Months
- No gender differences - Primary Safety and Primary Efficacy
- By Kaplan Meier estimate at 6 month: Primary Patency DCB - 86.3% / PTA - 72.2% (Δ14.0%, p=<0.001*)
- By Kaplan Meier estimate at 6 month: TLR Free DCB - 93.8% / PTA - 85.5% (Δ8.3 %, p=<0.004*)
- Reduction in the presence of any wound at 6 months compared to enrollment; no difference between DCB and PTA