Lutonix AV Clinical Trial

Long Term Effects of LUTONIX® 035 DCB Catheter 18 month Interim Results

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Disclosure

Speaker name: Scott O. Trerotola

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)

☐ I do not have any potential conflict of interest
Disclosures/Disclaimers

- The speaker’s presentation today is on behalf of C. R. Bard/LUTONIX, Inc. The physician has been compensated by Lutonix for the time and effort to present this information.
- Please consult Bard product labels and inserts relevant to your geography for indications, contraindications, hazards, warnings, cautions, and instructions for use.
- The opinions and clinical experiences presented herein are for informational and educational 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. Individual results may vary depending on a variety of patient specific attributes.
Agenda

• Fistula history and dysfunction
• LUTONIX® 035 DCB Catheter AV IDE Trial
  – Trial design
  – Primary efficacy/safety endpoint
  – 18 month IDE interim results
• Summary
History of Therapeutic Interventions for Hemodialysis Access

- 1966: First Surgical Fistula
- 1977: First Angioplasty
- 1983: First Published Data on PTA in Fistula
- 1997: KDOQI Guidelines Introduced
- 2005: First Large, Prospective Controlled, Randomized Cutting Balloon Trial: Peripheral Cutting Balloon™
- 2010: First Large, Prospective Controlled, Randomized Stent Graft Trial: FLAIR® Endovascular Stent Graft
- 2015: First Large, Prospective Controlled Randomized Stent Graft Trial: FLUENCY® PLUS Endovascular Stent Graft
- 2017: First in Fistula: Large, Prospective Controlled Randomized DCB Trial: LUTONIX® 035 PTA Catheter

51 Years
Lutonix AV Clinical Trial

Trial Design
# Lutonix AV IDE Clinical Trial

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Prospective, Global, Multicenter, Randomized, Safety and Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective</strong></td>
<td>To assess the safety and effectiveness of the LUTONIX® 035 AV Drug Coated Balloon PTA Catheter in the treatment of dysfunctional AV fistulae</td>
</tr>
<tr>
<td><strong>Number of patients/sites</strong></td>
<td>285 randomized subjects at 23 clinical sites</td>
</tr>
<tr>
<td><strong>Primary Effectiveness Endpoint</strong></td>
<td>Target Lesion Primary Patency (TLPP) - 6 months</td>
</tr>
<tr>
<td><strong>Primary Safety Endpoint</strong></td>
<td>Freedom from any serious adverse event(s) involving the AV access circuit through 30 days</td>
</tr>
<tr>
<td><strong>Follow Up</strong></td>
<td>1, 3, 6, 9, 12, 18, 24 month visits</td>
</tr>
</tbody>
</table>
| **Status** | First Subject: June 2015  
Enrollment Completion: March 2016 |
**Lutonix AV IDE Clinical Trial**

**Key Inclusion Criteria**

**CLINICAL CRITERIA**
- Male or non-pregnant female ≥21 years old
- Upper extremity AV Fistula w/clinical, physiological, or hemodynamic abnormality
- Fistula created ≥30 days
  - 1+ hemodialysis session
  - 2 needles
  - Catheter removed ≥30 days

**ANGIOGRAPHIC CRITERIA**
- Length ≤10 cm
- ≥50% stenosis
- Successful pre-dilation
- Diameter 4-12 mm

LU/9010//1017/0054a
Key Exclusion Criteria

**Clinical Criteria**
- Lower extremity access
- Central veins
- Thrombosed access

**Angiographic Criteria**
- >2 lesions in circuit
- Secondary non-target lesions that cannot be successfully treated
- Central veins as a secondary lesion, which is clinically significant
- Bare or covered stent in target or secondary non-target lesions
Lutonix AV IDE Clinical Trial

Study Design

Non-target lesion treated (if needed)
Residual stenosis ≤30%

Pre-Dilation with PTA

Pre-dilation lesion(s) treatment area criteria

Residual stenosis >30%
No enrollment in study
Further treatment per standard practice

Residual stenosis ≤30%
Completely efface waist
No clinical significant dissection/ extravsation
Randomization (1:1)
Enrollment in study

Treatment with Lutonix DCB (TEST)
≥ 1:1 Pre-Dil and test balloon sizing

Treatment with Standard PTA (CONTROL)
≥ 1:1 Pre-Dil and control balloon sizing

Follow-up: 1,3,6,9,12,18
and 24 months; unscheduled visits
Lutonix AV Clinical Trial

Demographic Data
Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>LUTONIX® 035 DCB (N=141)</th>
<th>Control (N=144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>63.6</td>
<td>61.0</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>61.7%</td>
<td>59.0%</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>94.3%</td>
<td>98.6%</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>58.2%</td>
<td>65.3%</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>60.3%</td>
<td>58.3%</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>13.5%</td>
<td>14.6%</td>
</tr>
<tr>
<td>Peripheral arterial disease, n (%)</td>
<td>9.9%</td>
<td>18.1%</td>
</tr>
<tr>
<td>Coronary heart disease, n (%)</td>
<td>30.5%</td>
<td>27.8%</td>
</tr>
</tbody>
</table>
Fistula Locations

Upper arm
DCB: 61.7% vs. PTA: 73.4%

Antecubital fossa
DCB: 5.0% vs. PTA: 4.9%

Forearm
DCB: 33.3% vs. PTA: 21.7%
## Lutonix AV IDE Clinical Trial

### Target Lesion Locations

<table>
<thead>
<tr>
<th>Location</th>
<th>DCB (n=141)</th>
<th>PTA (n=144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastomotic (%)</td>
<td>4.3%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Cephalic arch (%)</td>
<td>18.7%</td>
<td>22.5%</td>
</tr>
<tr>
<td>Cannulation zone (%)</td>
<td>4.3%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Inflow (%)</td>
<td>33.8%</td>
<td>29.6%</td>
</tr>
<tr>
<td>Outflow (%)</td>
<td>24.5%</td>
<td>22.5%</td>
</tr>
<tr>
<td>Swing point (%)</td>
<td>14.4%</td>
<td>12.0%</td>
</tr>
</tbody>
</table>
Lesion Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DCB (N=141)</th>
<th>PTA (N=144)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restenotic (%)</td>
<td>69.5%</td>
<td>72.9%</td>
</tr>
<tr>
<td>Tandem (%)</td>
<td>2.8%</td>
<td>7.0%</td>
</tr>
<tr>
<td>Mean target lesion length, mm (±SD)</td>
<td>28.4 ± 15.09</td>
<td>29.5 ± 18.69</td>
</tr>
</tbody>
</table>
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18 Month Interim Results
Data shown are interim, site reported and subject to change.

Primary Endpoint: Non-inferior to PTA

<table>
<thead>
<tr>
<th>Time Event (Days)</th>
<th>LTX DCB (N=141)</th>
<th>Standard PTA (N=144)</th>
<th>Difference % (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>545 Day Event Free</td>
<td>34.3% (4.7%)</td>
<td>22.6% (4.4%)</td>
<td>11.6% (6.4%)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Rate (SE)</td>
<td>(25.3%, 43.5%)</td>
<td>(14.7%, 31.6%)</td>
<td>(-0.9%, 24.2)</td>
<td></td>
</tr>
</tbody>
</table>

195% CI of the rate and the rate difference at each time point were calculated based on normal approximation and one-sided p-value is from test for non-inferiority, with 10% as non-inferiority margin.

LU/9010//1017/0054a
Target Lesion Primary Patency (TLPP) ends with a clinically driven re-intervention of the target lesion or access thrombosis. 95% CI of the rate and rate difference at each time point were calculated based on normal approximation using Greenwood formula variance estimators. Log-Rank Test was used to compare the two treatment curves between Day 0-210 and one-sided p-value was provided.

<table>
<thead>
<tr>
<th>Time to Event</th>
<th>LTX DCB (N=141)</th>
<th>Standard PTA (N=144)</th>
<th>Difference % (95% CI)</th>
<th>P-value¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>180 Day Event Free</td>
<td>71.4% (4.0%)</td>
<td>63.0% (4.1%)</td>
<td>8.4% (5.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Rate (SE)</td>
<td>(62.7%, 78.4%)</td>
<td>(54.4%, 70.4%)</td>
<td>(-2.8%, 19.6%)</td>
<td></td>
</tr>
<tr>
<td>210 Day Event Free</td>
<td>64.1% (4.3%)</td>
<td>52.5% (4.3%)</td>
<td>11.6% (6.0%)</td>
<td>0.024</td>
</tr>
<tr>
<td>Rate (SE)</td>
<td>(55.1%, 71.8%)</td>
<td>(43.9%, 60.5%)</td>
<td>(-0.2%, 23.4%)</td>
<td></td>
</tr>
</tbody>
</table>

*one-sided p-value

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Target Lesion Primary Patency (TLPP) ends with a clinically driven re-intervention of the target lesion or access thrombosis. 95% CI of the rate and rate difference at each time point were calculated based on normal approximation using Greenwood formula variance estimators. Log-Rank Test was used to compare the two treatment curves between Day 0-550 and one-sided p-value was provided.

<table>
<thead>
<tr>
<th></th>
<th>LTX DCB (N=141)</th>
<th>Standard PTA (N=144)</th>
<th>Difference % (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>545 Day Event Free</td>
<td></td>
<td></td>
<td></td>
<td>0.038</td>
</tr>
<tr>
<td>Rate (SE)</td>
<td>35.7% (5.4%)</td>
<td>26.1% (4.8%)</td>
<td>9.6% (7.2%)</td>
<td></td>
</tr>
<tr>
<td>95% CI</td>
<td>(25.3%, 46.3%)</td>
<td>(17.3%, 35.7%)</td>
<td>(-4.5%, 23.8%)</td>
<td></td>
</tr>
</tbody>
</table>
## Lutonix AV IDE Clinical Trial

### Number of Interventions Required to Maintain TLP

<table>
<thead>
<tr>
<th></th>
<th>LTX DCB (n=141)</th>
<th>Standard PTA (n=144)</th>
<th>P-value*</th>
<th>% Fewer Interventions than PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of interventions, 180 days</td>
<td>44</td>
<td>64</td>
<td>0.068</td>
<td>31.3% Fewer</td>
</tr>
<tr>
<td>Number of interventions, 210 days</td>
<td>58</td>
<td>86</td>
<td>0.022</td>
<td>32.6% Fewer</td>
</tr>
</tbody>
</table>

*Two-sided P-value
Lutonix AV IDE Clinical Trial
Summary

• First and only DCB with 18 month Level 1 Data in AVF
• Safety outcomes are non-inferior to PTA
• Sustained effectiveness benefit
  – 71.4% target lesion primary patency (TLPP) at 6 months
  – 31.3% fewer number of interventions required to maintain TLP at 6 months
  – 36.8% improvement in TLPP over PTA at 18 months
• Interim 24-month results
  • Thursday, 15:59-16:04pm, Room 1, Main Arena 1
• Next step: Post Approval Study

Data shown are interim, site reported and subject to change
Thank You
INDICATIONS FOR USE
The Lutonix® 035 Drug Coated Balloon Catheter is intended for Percutaneous Transluminal Angioplasty (PTA) in the peripheral vasculature and for the treatment of obstructive lesions and decreasing the incidence of restenosis. In addition, the Lutonix® 035 Drug Coated Balloon Catheter is intended for PTA of native dialysis fistulae or synthetic grafts, opening narrowing and immature fistulae, to improve blood flow, and decreasing the incidence of restenosis.

CONTRAINDICATIONS
- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children over the next 2 years. 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.
- 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 after the “Use by” date.
- 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 as this may cause air emboli in case of balloon burst. This product should not be used in patients with known hypersensitivity to paclitaxel or structurally related compounds as this may cause allergic reaction (difficulty in breathing, skin rash, muscle pain).
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18 month Interim Results

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