New Insights from Levant 2
Randomized Data, Sub Group and Post Hoc Analysis
Disclosure

Speaker name:
Dr. Dierk Scheinert

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
Lutonix: The Science
Anatomy of DCB Balloon

Drug + Carrier = COATING

- All DCBs use Paclitaxel
- Paclitaxel differs from DCB to DCB:
  - Crystalline
  - Amorphous

- Important to bind paclitaxel to the balloon
- Differs from manufacturer to manufacturer

- KEY REQUIREMENTS:
  - Drug Uniformity
  - Drug Retention
  - Drug Release
Lutonix® DCB Formulation

• Result of extensive development and rigorous testing
  • 45 pre-clinical studies
  • >11,000 histology samples

• Resulted in an optimized formulation with a therapeutic dose of 2 µg/mm²
Lutonix: The Technology
Lutonix Coating: Drug Uniformity

Coating Uniformity Analysis*

<table>
<thead>
<tr>
<th></th>
<th>± 4.0%</th>
<th>± 2.7%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segment-to-Segment Variability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Longitudinal Segment Variability</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Consistent variance across all Lutonix balloons

*Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.
Lutonix Coating: Drug Delivery

In Vivo Administration of Fluorescent-Labeled PTX to Excised Porcine Artery

10% Oregon green labeled paclitaxel incorporated into Lutonix® DCB coating

Uniform Delivery in vivo at 1 hour
(Animal vessel cross section after 30 sec. inflation)

Lutonix coating uniformity allows uniform drug delivery
Lutonix Coating Durability

Dry Inflate “Shake” Test

<table>
<thead>
<tr>
<th>Residual Drug on DCB Balloon After Inflation/Shake</th>
<th>Drug Loss After DCB Inflation/Shake</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTX DCB (n=5)</td>
<td>99.4% ± 1.1%</td>
</tr>
</tbody>
</table>

Evidence of Durability.

*Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.
Lutonix Coating: Drug Retention

Drug load preserved on balloon post-insertion through sheath valve or tuohy

Durability of coating preserved through insertion

*Terumo Pinnacle Destination

*Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.
Lutonix Coating Durability*

Simulated Clinical Use Test LUTONIX®

Amount of drug lost on the back table. (Drug measured- ng/mg)

Designed to minimize unnecessary drug exposure to staff and patients

*Bench test data on file. Bench results may not be indicative of clinical performance. Different test methods may yield different results.
Lutonix Coating Durability

Lutonix 035

IN.PACT

Designed to minimize unnecessary drug exposure to staff and patients

Data on file
New Insights from Levant 2: Randomized Data, Sub Group and Post Hoc Analysis
<table>
<thead>
<tr>
<th>Angiographic Characteristics (ITT)</th>
<th>Lutonix DCB (316)</th>
<th>Standard PTA (160)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two lesions treated</td>
<td>1.9% (6/316)</td>
<td>3.1% (5/160)</td>
<td>0.400</td>
</tr>
<tr>
<td>Total Lesion Length (mm)</td>
<td>62.7 ± 41.4 (315)</td>
<td>63.2 ± 40.4 (160)</td>
<td>0.900</td>
</tr>
<tr>
<td>Treated Length (mm)</td>
<td>107.9 ± 47.0 (316)</td>
<td>107.9 ± 49.4 (160)</td>
<td>0.988</td>
</tr>
<tr>
<td>Calcification</td>
<td>59.2% (187/316)</td>
<td>58.1% (92/160)</td>
<td>0.826</td>
</tr>
<tr>
<td>Total Occlusion</td>
<td>20.6% (65/316)</td>
<td>21.9% (35/160)</td>
<td>0.741</td>
</tr>
<tr>
<td>Re-stenotic Lesions</td>
<td>16.1% (51/316)</td>
<td>12.5% (20/160)</td>
<td></td>
</tr>
<tr>
<td>Lesion Locations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SFA</td>
<td>90% (285/316)</td>
<td>92.5% (148/160)</td>
<td></td>
</tr>
<tr>
<td>Proximal Popliteal</td>
<td>4.7% (15/316)</td>
<td>4.4% (7/160)</td>
<td></td>
</tr>
<tr>
<td>Mid &amp; Distal Popliteal</td>
<td>5.0% (16/316)</td>
<td>3.1% (5/160)</td>
<td></td>
</tr>
<tr>
<td>%DS post-treatment</td>
<td>23.4 ± 12.3 (316)</td>
<td>23.8 ± 12.3 (158)</td>
<td>0.703</td>
</tr>
<tr>
<td>Bail-out Stenting</td>
<td>2.5% (8/316)</td>
<td>6.9% (11/160)</td>
<td>0.022</td>
</tr>
<tr>
<td>Dissection</td>
<td>63.7% (200/314)</td>
<td>72.3% (115/159)</td>
<td>0.060</td>
</tr>
</tbody>
</table>
Primary Patency Kaplan-Meier

Survival %

<table>
<thead>
<tr>
<th>Time</th>
<th>Lutonix DCB</th>
<th>Standard PTA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>365 days</td>
<td>73.5%</td>
<td>56.8%</td>
<td>0.001</td>
</tr>
</tbody>
</table>

$\Delta = 16.7\%$ (~30% Improvement over PTA)
A post-hoc subgroup analysis suggests the full wall apposition of the Lutonix® 035 Drug Coated Balloon (minimum 1.04:1 balloon-to-artery ratio of the treatment device) showed increased primary patency of 79.9% (Kaplan Meier, not pre-specified). Primary patency is defined as absence of binary restenosis defined by DUS PSVR ≥2.5 and freedom from Target Lesion Revascularization (TLR). Primary safety by treatment balloon / artery ratio <1 was 85.8% (DCB) and 82.1% (PTA). Primary safety by treatment balloon / artery ratio >1 was 79.3% (DCB) and 75.5% (PTA). **Warning: Do not exceed Rated Burst Pressure.**
Lutonix DCB Effective in Calcified Lesions

<table>
<thead>
<tr>
<th>Survival %</th>
<th>Time</th>
<th>Lutonix DCB</th>
<th>Standard PTA</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>365 days</td>
<td>75.4%</td>
<td>55.7%</td>
<td>0.018</td>
</tr>
</tbody>
</table>

Kaplan Meier analysis, 38 events 67 at risk
Sub Group analysis. Study endpoint not powered for statistical significance, not adjusted for multiplicity
Lutonix DCB Effective in Diabetic Patients

Kaplan Meier analysis, 42 events 107 at risk
Sub Group analysis. Study endpoint not powered for statistical significance
“Stent Like TLR”

Lutonix DCB freedom from TLR rate of 89.7% is consistent with current stent freedom from TLR rates

Kaplan-Meier Analysis from public data – results as reported in different studies, with different protocols and different patient population. Not intended for head to head comparisons.
Reported Patient Benefits
WIQ Walking Distance

Sub Group analysis. Study endpoint not powered for statistical significance
Reported Patient Benefits

Improvement in Rutherford Class

82.7% Lutonix DCB Patients Reported Sustained Improvement in Rutherford Class compared to 73.4% with PTA

<table>
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<th>Time</th>
<th>Lutonix DCB</th>
<th>Standard PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>365 days</td>
<td>82.7%</td>
<td>73.4%</td>
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</table>

Sub Group analysis. Study endpoint not powered for statistical significance
Freedom from Primary Safety Event

Survival %

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<thead>
<tr>
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<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>365 days</td>
<td>86.7%</td>
<td>81.5%</td>
<td>0.185</td>
</tr>
</tbody>
</table>

DTA
DCB
Lutonix DCB
PTA
Standard PTA
## Other Secondary Safety Endpoints

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lutonix DCB n/N (%)</th>
<th>Standard PTA n/N (%)</th>
<th>Difference % [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite Safety Events</td>
<td>240/286 (83.9%)</td>
<td>113/143 (79.0%)</td>
<td>4.9% [-3.0, 12.8]</td>
</tr>
<tr>
<td>Death</td>
<td>7/290 (2.4%)</td>
<td>4/144 (2.8%)</td>
<td>-0.4% [-3.6, 2.8]</td>
</tr>
<tr>
<td>Major Amputation</td>
<td>1/286 (0.3%)</td>
<td>0/140 (0.0%)</td>
<td>0.3% [-0.3, 1.0]</td>
</tr>
<tr>
<td>Rate of embolism</td>
<td>1/316 (0.3%)</td>
<td>1/160 (0.3%)</td>
<td>—</td>
</tr>
<tr>
<td>Reintervention for Thrombosis</td>
<td>1/285 (0.4%)</td>
<td>1/140 (0.7%)</td>
<td>-0.4% [-1.9, 1.2]</td>
</tr>
</tbody>
</table>
Effectiveness Without Compromising Safety

• Levant 2 demonstrated superior patency for Lutonix DCB against PTA
  – ~ 80% patency with correct DCB/RV ratio Angioplasty*
  – Lutonix DCB effective in Calcified lesions and Diabetic patients
  – Stent like Freedom from TLR rates of 89% and is consistent with Real-World Registry

• Levant 2 demonstrated safety of Lutonix DCB
  – Low rates of re-intervention for thrombosis and embolism
  – No unanticipated safety events in over 1000 patients**

• Patients who received Lutonix DCB reported Clinical Benefits in Levant 2
  – Sustained improvement in Rutherford Class
  – Improvement in self-reported Walking Distance scores

* Post-hoc, subgroup analysis, Kaplan Meier
** Levant 2 roll-ins, Levant 2 randomized trials and Levant 2 Continued Access Registry