DCB: What Is The Evidence?

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Medical Director Vascular Medicine
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What is the Pathway to Follow

Timeline of First-in-Man to Product Approval to PMR data: 5-7 Years!!
An Effective DCB Catheter Formulation Should...

- Use the lowest possible dose needed to achieve therapeutic tissue levels
- Retain drug on the balloon during transit to the lesion
- Ensure rapid drug transfer upon balloon inflation
- Produce a uniform, durable, transfer efficient coating
- Demonstrate histologic “Drug-Effect” at least 28 days post treatment by light microscopy in preclinical models as the experience from DES is extensive
• Drug-load balloon with 2µg per mm² of paclitaxel
• IV approved carriers of polysorbate & sorbitol
• Uniform coating

Manufacturer: Lutonix, Inc., a subsidiary of C. R. Bard
**LUTONIX® Optimized Coating Formulation Showed Favorable Downstream Safety in a Porcine Model**

**At 1x and 4x Doses:**

- No physiologically significant changes observed at 1x and 4x doses at 28, 90, and 180 Days.
  - Very rare focal changes observed in small arterioles
  - No embolic-occlusive events or particulate observed
  - No skeletal muscle necrosis observed
LUTONIX® DCB Catheter Technology

**Uniform**
- Coating applied while balloon is inflated
- <0.1% drug loss after dry inflate test*
- <0.1% drug loss after sheath insertion

<table>
<thead>
<tr>
<th>Coating Uniformity Analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Segment-to-Segment Variability</strong></td>
</tr>
<tr>
<td><strong>Coating Variability:</strong></td>
</tr>
</tbody>
</table>

*Consistent variance across all LUTONIX® balloons


Data on file at Lutonix
Ex Vivo Administration of Fluorescent-Labeled PTX to Excised Porcine Artery

10% Oregon green labeled paclitaxel incorporated into Lutonix DCB coating
1. **30 second** minimum inflation
   transfers drug to endoluminal surface delivering a therapeutic dose
2. PTX diffuses into the arterial wall from an endoluminal reservoir
3. Over time, therapeutic drug levels are sustained in deep cell layers after endothelial drug levels become sub-therapeutic
4. Drug continues to inhibit restenosis in arterial wall while allowing the lumen to restore and re-endothelialize
A Brief History of BTK/CLI Data on DCBs

- Leipzig BTK Registry (3 Month data) published
- DEBATE BTK (12 month data) Published
- MDT Recalls IN.PACT Amphirion DCB
- In.PACT DEEP Results Presented

All data from IN.PACT Amphirion Deep DEB
Leipzig Registry
Schmidt et al. JACC 2011;58:1105-9

- **Design**
  - Single-Center
  - \( N=104 \) (enrolled Jan 2009-Feb 2010)

- **Procedural Methods**
  - Inflation for \( \geq 1 \) min
  - In case of 2+ DCBs, balloon overlap = 5mm
  - Inflow disease treated during same session \((n = 28 \) limbs, proximal PTA)
  - DAPT for at least 4 weeks post-op

- **Patient Population**
  - 82.6% with CLI
  - Mean lesion length = 17.6cm
  - 55 de novo, 19 restenoses, 10 in-stent-restenoses
  - Renal Insufficiency = 46.2%
  - Diabetes = 71.1%
  - Smoking = 30.8%
Leipzig Registry Cont’d
Schmidt et al. JACC 2011;58:1105-9

- **Interventional Success = 100%**
  - 5 bail-out stents placed
  - *Pre-discharge complications = 3 femoral pseudoaneurysms and 1 infected diabetic foot*
- **3-Month follow-up (n=94 patients)**
  - *Angiography f/u (n=74 patients)*
    - 72.6% (61/84 arteries) were free of significant restenosis
      » 61% of restenosis were focal (<20% of initial length)
  - *3-Month restenosis rate considerably lower than center’s historical data: 27% vs. 69%*
- **No Safety concerns**
  - **Amputation rate: 4.4% (typical for population)**
DEBATE-BTK

- **Study Design**
  - Single-center (Italy), RCT 1:1
  - No Core lab
- **Key Inclusion Criteria:**
  - CLI and diabetes
  - At least one tibial vessel run-off
- **Key Exclusion**
  - Allergy to PTX
  - Life expectancy < 1 year
- **Primary endpoint:** Binary restenosis at 1 year
- **Secondary Endpoints:** 12-Month TLR and 12-Month Occlusion rate
DEBATE-BTK Cont’d

<table>
<thead>
<tr>
<th>Baseline Demographics</th>
<th>DEB</th>
<th>PTA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td># Lesions</td>
<td>80</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>100%</td>
<td>100%</td>
<td>1</td>
</tr>
<tr>
<td>Dialysis</td>
<td>10.8%</td>
<td>10.4%</td>
<td>1</td>
</tr>
<tr>
<td>Inflow Treatment</td>
<td>49.2%</td>
<td>52.2%</td>
<td>0.8</td>
</tr>
<tr>
<td>Mean Lesion Length (mm)</td>
<td>129</td>
<td>131</td>
<td>0.9</td>
</tr>
<tr>
<td>Severe Calcification</td>
<td>25%</td>
<td>28%</td>
<td>0.5</td>
</tr>
<tr>
<td>Sub-intimal Recanalization</td>
<td>21.3%</td>
<td>21.8%</td>
<td>0.8</td>
</tr>
</tbody>
</table>

• **Procedural Characteristics**
  • 100% Pre-dil in DCB group
  • Mean inflation time 142 secs
  • 1 bail-out stent placed (1.3%)
# DEBATE-BTK 1 Year Clinical Outcomes


<table>
<thead>
<tr>
<th>1-Year Clinical Outcomes</th>
<th>DEB</th>
<th>PTA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (any cause)</td>
<td>7.7% (5)</td>
<td>4.5% (3)</td>
<td>0.4</td>
</tr>
<tr>
<td>Major Amputation</td>
<td>0</td>
<td>1.5% (1)</td>
<td>0.9</td>
</tr>
<tr>
<td>Binary Restenosis</td>
<td>27% (20/74)</td>
<td>74.3% (55/74)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>TLR</td>
<td>15% (12/80)</td>
<td>37% (29/78)</td>
<td>0.002</td>
</tr>
<tr>
<td>Complete ulcer healing</td>
<td>86% (56/65)</td>
<td>37% (43/64)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Authors’ conclusions: “DCBs compared with PTA strikingly reduce 1-year restenosis, TLR and target vessel occlusion in the treatment of BTK lesions in diabetic patients with CLI”
### DEBATE-BTK Two-Year Clinical Outcomes

#### Liistro LINC 2014

<table>
<thead>
<tr>
<th></th>
<th>DEB</th>
<th>PTA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death (any cause)</td>
<td>18.5% (12)</td>
<td>16.5% (11)</td>
<td>0.8</td>
</tr>
<tr>
<td>Major Amputation</td>
<td>1.4% (1)</td>
<td>2.8% (2)</td>
<td>1</td>
</tr>
<tr>
<td>TLR</td>
<td>17.5% (14/80)</td>
<td>41% (32/78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lesions w/ &gt; 1 TLR</td>
<td>2% (2)</td>
<td>11% (9)</td>
<td>0.03</td>
</tr>
<tr>
<td>MAE</td>
<td>36% (24)</td>
<td>52% (37)</td>
<td>0.05</td>
</tr>
<tr>
<td>New restenosis 12-24 months</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Cumulative restenosis</td>
<td>30% (24/80)</td>
<td>78% (61/78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Secondary Patency</td>
<td>92% (61/66)</td>
<td>64% (39/61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Complete wound healing</td>
<td>93% (53/57)</td>
<td>86% (48/56)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions:
- Advantages of DCB observed at 12 months, were maintained at 2 years
- Study provides evidence for use of DEB in diabetic patients with CLI
Challenges of Single-Center Studies

- Mirror’s specific center’s practice
- Lower external validity
- Limited generalizability
- Typically lacks core lab or CEC adjudication
- Value in generating hypotheses

Large, robust studies are essential.
IN.PACT DEEP
Thomas Zeller, LINC 2014

• **Study Design**
  – Prospective, multi-center, randomized,
  – Rigorous execution: independent DCMB, CEC, angiographic and wound core labs, external monitoring with 100% source data verification
  – \( N = 358 \) subjects, enrolled Sep 2009-July 2012 at 13 centers in 6 EU countries
  – Primary effectiveness endpoints:
    • Angio Cohort: Late lumen loss at 12 months or time of TLR
    • All patients: Clinically-driven TLR at 12 months
  – Primary Safety Endpoint: 6-month all-cause death, major amputation or clinically-driven TLR
IN.PACT DEEP Selection Criteria

- **Key Inclusions**
  - RCC 4,5,6
  - Target Vessel: infrapop (including TPT) above ankle
  - RVD 2-4 mm
  - At least 1 non-occluded crural vessel w/run-off to the foot either direct or through collaterals
  - Single or multiple adjacent lesions (≥70%) with cumulative length of ≤10 cm that can be covered by a single IN.PACT Amphirion DCB

- **Key Exclusions**
  - Planned major index limb amputation
  - Inflow impaired or non re-established
  - Failure to cross the target lesion with a 0.014” guide wire
  - In-stent-restenosis
  - Thrombus or aneurysm
  - GFR < 30ml/min except for patients with ESRD on chronic haemodialysis
## IN.PACT DEEP Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DEB</th>
<th>PTA</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>73.3 ± 8.2</td>
<td>71.7 ± 9.9</td>
<td>0.106</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>72.6%</td>
<td>70.6%</td>
<td>0.304</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>75.7%</td>
<td>68.9%</td>
<td>0.204</td>
</tr>
<tr>
<td><strong>Renal Insufficiency (GFR &lt; 30 ml/min)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Current Smoker</strong></td>
<td>15.1%</td>
<td>13.4%</td>
<td>0.752</td>
</tr>
<tr>
<td><strong>ABI</strong></td>
<td>0.75</td>
<td>0.81</td>
<td>0.264</td>
</tr>
<tr>
<td><strong>TBI</strong></td>
<td>0.32</td>
<td>0.46</td>
<td>0.178</td>
</tr>
</tbody>
</table>

![Pie charts showing distribution of RC categories for DEB and PTA cohorts.]

**RC 5:** 84.1% for DEB Cohort

**RC 5:** 77.3% for PTA Cohort

**RC 4:** 17.6% for PTA Cohort

**RC 4:** 14.2% for DEB Cohort

**RC 3:** 0.8% for PTA Cohort

**RC 3:** 0.8% for DEB Cohort
### IN.PACT DEEP Baseline Angiographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DEB</th>
<th>PTA</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions</td>
<td>351</td>
<td>181</td>
<td>0.443</td>
</tr>
<tr>
<td>Impaired Inflow (≥50%)</td>
<td>40.7% (96/236)</td>
<td>28.8% (34/118)</td>
<td>0.035</td>
</tr>
<tr>
<td>Heavy Calcium</td>
<td>13.7%</td>
<td>10.5%</td>
<td>0.332</td>
</tr>
<tr>
<td>Moderate Calcium</td>
<td>51.1%</td>
<td>57.5%</td>
<td></td>
</tr>
<tr>
<td>Target Lesion Length (cm)</td>
<td>10.2</td>
<td>10.9</td>
<td>0.002</td>
</tr>
<tr>
<td>Inflation time (secs)</td>
<td>166</td>
<td>137</td>
<td></td>
</tr>
</tbody>
</table>
## IN.PACT DEEP Procedural Characteristics

<table>
<thead>
<tr>
<th></th>
<th>DEB (%)</th>
<th>PTA (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Dilatation</td>
<td>90.5</td>
<td>36.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inflation time (secs)</td>
<td>166</td>
<td>137</td>
<td>0.010</td>
</tr>
<tr>
<td>Max Inflation Pressure (atm)</td>
<td>9.5</td>
<td>10.3</td>
<td>0.010</td>
</tr>
<tr>
<td>Stenting</td>
<td>3.9</td>
<td>2.6</td>
<td>0.446</td>
</tr>
<tr>
<td>Procedural complications (excluding post proc. dissections)</td>
<td>9.7</td>
<td>3.4</td>
<td>0.035</td>
</tr>
<tr>
<td>Post-procedure dissections</td>
<td>12.3</td>
<td>19.2</td>
<td>0.046</td>
</tr>
<tr>
<td>Device Success$^1$</td>
<td>98%</td>
<td>96.3%</td>
<td>0.224</td>
</tr>
<tr>
<td>Procedural success$^2$</td>
<td>98.3%</td>
<td>100%</td>
<td>0.155</td>
</tr>
</tbody>
</table>

1. Device Success: exact deployment of the device according to the IFU as documented with suitable imaging modalities
2. Procedural success: successful vascular access and completion of procedure with ≤ 50% residual stenosis by angio, and device success in the absence of procedural complications.
## IN.PACT DEEP Primary Outcomes

<table>
<thead>
<tr>
<th>Primary Efficacy</th>
<th>DEB</th>
<th>PTA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-month LLL (mm)</td>
<td>0.61± 0.78</td>
<td>0.62± 0.78</td>
<td>0.950</td>
</tr>
<tr>
<td>12-month Clinically-driven TLR</td>
<td>9.2% (18/196)</td>
<td>13.1% (14/107)</td>
<td>0.291</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary Safety</th>
<th>DEB</th>
<th>PTA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-month Death, major amputation or Clinically-driven TLR</td>
<td>17.7% (41/232)</td>
<td>15.8% (18/114)</td>
<td>0.021 (non-inferiority) 0.662 (superiority)</td>
</tr>
</tbody>
</table>

Did not meet either primary efficacy endpoints
## IN.PACT DEEP Secondary Outcomes

<table>
<thead>
<tr>
<th>Primary Efficacy</th>
<th>DEB</th>
<th>PTA</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Amputation</td>
<td>8.8% (20/227)</td>
<td>3.6% (4/111)</td>
<td>0.080</td>
</tr>
<tr>
<td>All-cause Mortality</td>
<td>10.1% (23/227)</td>
<td>8.1% (9/111)</td>
<td>0.551</td>
</tr>
<tr>
<td>Death and Amputations</td>
<td>35.2% (80/227)</td>
<td>25.2% (28/111)</td>
<td>0.064</td>
</tr>
<tr>
<td>Death, Major Amp, CD TLR</td>
<td>26.9% (61/227)</td>
<td>23.4% (26/111)</td>
<td>0.496</td>
</tr>
<tr>
<td>Amputation-Free Survival</td>
<td>81.1% (184/227)</td>
<td>89.2% (99/111)</td>
<td>0.057</td>
</tr>
<tr>
<td>Wound Healing (site reported)</td>
<td>73.8% (121/164)</td>
<td>76.9% (70/91)</td>
<td>0.579</td>
</tr>
</tbody>
</table>
IN.PACT DEEP Conclusions

- First large, randomized, level 1 evidence clinical trial of DCB for BTK CLI
- Did not meet either primary effectiveness endpoint
  - PTA outcomes were significantly better than expected
- Met the non-inferiority primary safety endpoint
- Study findings are limited to BTK CLI indication and IN.PACT Amphirion DEB
- Patients will be followed for 5 years
Where do we go from here?
Up-coming Level-1 Data

**Bard: LEVANT BTK Study**
- Multi-center, RCT, IDE study
- Now enrolling in the US, EU and Japan
- N= 480 patients,
  - randomized 2:1 btwn Lutonix DCB vs. PTA

**BEST-CLI Study**
- NIH-funded, prospective, RCT of 2,100 CLI patients
- 5 year follow-up
- 80 US and Canadian sites
- Enrollment will begin Q2 2014
# Trial Summary

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

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

## FOLLOW-UP
- **Clinical:** 1, 6, 12, 24, and 36 Months
- **Duplex Ultrasound (DUS):** 0–30 days, 6, 12, 24, & 36 months
- **Angiography in subset of patients:** 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
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.

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

### 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 1.73m²
- 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

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Caution – Investigational Device, Limited by Federal (USA) Law to Investigational Use
## Current DCB Available

<table>
<thead>
<tr>
<th>Company</th>
<th>Drug/Drug Dose</th>
<th>Delivery Matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elutax) (Aachen Resonance)</td>
<td>Paclitaxel 2.2 µg/mm²</td>
<td>Uses ICE &amp; SNOW technology (layering of paclitaxel). ICE = elastic, stable ground layer. On top, SNOW layer = drug depot. No excipient is used.</td>
</tr>
<tr>
<td>In.Pact Pacific (Medtronic)</td>
<td>Paclitaxel 3.0 µg/mm²</td>
<td>FreePac™, a hydrophilic coating with urea (100% natural component) that frees and separates paclitaxel molecules</td>
</tr>
<tr>
<td>LUTONIX® (BARD)</td>
<td>Paclitaxel 2.0 µg/mm²</td>
<td>Polysorbate and sorbitol. Coating evenly distributed across the working length of the balloon.</td>
</tr>
<tr>
<td>Freeway™ (Eurocor)</td>
<td>Paclitaxel 3.0 µg/mm²</td>
<td>Bioshell, a matrix that consists of paclitaxel and shellac, a natural resin composed of shelloic and alleuritic acid.</td>
</tr>
<tr>
<td>Legflow OTW® (Cardionovum®)</td>
<td>Paclitaxel 3.0 µg/mm²</td>
<td>PTX-BOLUS-DRUG Coating Technology, a high density paclitaxel dose applied between two layers of shelloic acid.</td>
</tr>
<tr>
<td>Biotronik</td>
<td>Paclitaxel 3.0 µg/mm²</td>
<td>Paclitaxel and Butyl-tri-hexyl citrate (BTHC) as excipient</td>
</tr>
</tbody>
</table>
Coating: Is it Relevant?

• The drug coating is designed to be robust
  – Adhere to the balloon substrate during the manufacturing process
  – To prevent delamination during handling in a clinical environment before introduction into the blood stream.
  – Durability of the drug coating is also important to maintain the drug content label claim of the product.
Aim and Methods

• To determine coating durability on DCB products commercially available in Europe.

• Two known methods selected for this evaluation:
  – The Dry Inflate/Shake Test (Published by Kelsch 2011)
  – The Simulated Clinical Use Wipe Test
The Dry Inflate/Shake Test
Kelsh

• This test method involves removing each drug coated balloon (DCB) from its packaging, including the balloon protector.

• The balloon is then inserted into a centrifuge tube, inflated with air, and then shaken five (5) times against the inside wall of the tube.

• The balloon is then transferred from this 1st tube (#1) into a 2nd centrifuge tube (#2) and cut from the catheter shaft to allow analytical testing to be performed.

• Each DCB generates two (2) sample tubes where one sample (#1) is comprised of the amount shaken off and the other tube (#2) contains the DCB and remaining coating.
The Dry Inflate/Shake Test - BTK

- Test Articles (n=5 each, 3x80mm):
  - Lutonix® 014 DCB
  - MDT In.Pact Amphirion
  - Medrad Cotavance DCB
  - Cardionovum Legflow DCB
  - Eurocor Freeway DCB
  - Aachen Resonance Elutax SV

Dry Inflate/Shake Test - 'Shaken off' Material (n=5)

<table>
<thead>
<tr>
<th>Material</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lutonix® 014</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td>MDT In.Pact Amphirion</td>
<td>25.3%</td>
</tr>
<tr>
<td>Medrad</td>
<td>27.1%</td>
</tr>
<tr>
<td>Cardionovum</td>
<td>4.6%</td>
</tr>
<tr>
<td>Eurocor</td>
<td>1.4%</td>
</tr>
<tr>
<td>Aachen Resonance Elutax SV</td>
<td>3.3%</td>
</tr>
</tbody>
</table>
The Dry Inflate/Shake Test - SFA

- Test Articles (n=5 each):
  - Medtronic In.Pact Admiral – 6x60mm
  - Lutonix® 035 Drug Coated Balloon – 6x60mm

**Dry Inflate/Shake Test - 'Shaken off' Material**
(n=5)

- Lutonix® 035
- MDT In.Pact Admiral

- Lutonix® 035: 0.1%
- MDT In.Pact Admiral: 10.6%
Medtronic

Lutonix
The Dry Inflate/Shake Test

• The highest amount of paclitaxel that did not adhere to the BTK devices were from Medrad and Medtronic.
• The Lutonix® DCB released the least in both tests
• Both MDT and LTX samples were then tested in the next test protocol: Simulated Use Wipe Test Method
The Simulated Clinical Use Test

• **Test Objective:**
  – Evaluate the amount of paclitaxel that does not adhere to the balloon and is transferred to work surfaces during simulated clinical procedural handling.

• **Test Articles (n=3 per physician for both SFA and BTK):**
  – Lutonix® DCB and Medtronic DCB

• **Test Subjects:**
  – Three (3) independent physicians at three hospitals

• **Test Protocol:**
  – Sterile collection drape placed over work surface
  – DCB removed from packaging, Balloon Protector removed above drape and DCB loaded onto guidewire and passed through Introducer Sheath
  – The drape is then swabbed along with the physicians gloves for residual paclitaxel
  – NOTE: The technician performing the swabbing was blinded to the Test Article.
The Simulated Clinical Use Test

• **Test Materials and Analysis:**
  
  – Swabs used were from ChemoGLO™ (commercially available testing kit that accurately quantifies trace amounts of drug contaminants in the work environment)
  
  – Swab samples sent to an independent lab (ChemoGlo™) for analysis
  
  – The paclitaxel surface concentrations in the ChemoGLO™ analysis reports were calculated based on 1 ft$^2$ of area. The actual wipe surface area in this study as described in the protocol was 5 ft$^2$ (4645cm$^2$). Results are reported are corrected for this.
  
  – The lowest limits of quantization (LLQ) of the method are 10.0 ng/ft$^2$ and 0.01 ng/cm$^2$
The Simulated Clinical Use Test

- One-Way ANOVA statistical analysis of overall Lutonix compared to Medtronic

<table>
<thead>
<tr>
<th>Devices</th>
<th>Sample Size</th>
<th>Average Paclitaxel Conc. (ng/cm²)</th>
<th>Standard deviation</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lutonix 6x120mm</td>
<td>21</td>
<td>0.34</td>
<td>0.27</td>
<td></td>
</tr>
<tr>
<td>Medtronic 6x120mm</td>
<td>18</td>
<td>20.39</td>
<td>17.15</td>
<td>p=0.00</td>
</tr>
</tbody>
</table>
Not All DCB’s Are The Same!

LUTONIX

IN.PACT FALCON

PANTERA LUX

SEQUENT PLEASE