Drug-Eluting Balloons: A New Era in SFA Rx

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NCVH 2017
Atherosclerosis

“A man is as old as his arteries”

Thomas Sydenham, 1624-1689
Forces simulated in SFA

Radial Compression

Longitudinal Compression / Extension

Flexion

Torsion
Treatment Options

- PTA
- Drug Coated Devices
- Stent
  - Types
  - Complications
- Atherectomy
  - Laser
  - Directional
  - Orbital
  - Cryo
  - Contact
How to Select?

- Debulking strategy
- Effective luminal widening
- In limb salvage, likely effective
- Durability not well documented
- Cost of therapy
- Several approaches:
  - Directional (silverhawk)
  - Rotational: CSI, Pathway
- Distal Embolization higher than with PTA
Drug Eluting Balloon
“Leave no metal behind”
## In.Pact: Formulation

### DCB Components

<table>
<thead>
<tr>
<th>Component</th>
<th>IN.PACT™ Admiral™ DCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA Balloon</td>
<td>Admiral™ PTA balloon 4-7 mm diameters</td>
</tr>
<tr>
<td></td>
<td>40, 60, 80, 120 mm lengths</td>
</tr>
<tr>
<td>Paclitaxel</td>
<td>Proven anti-proliferative drug 3.5 µg/mm²</td>
</tr>
<tr>
<td>Urea</td>
<td>Facilitates drug transfer Naturally occurring, non-toxic</td>
</tr>
<tr>
<td>Medtronic</td>
<td>Reliable, scalable, uniform drug coating process</td>
</tr>
</tbody>
</table>

### Platform

- Platform

### Drug

- Drug
- Paclitaxel

### Excipient

- Excipient
- Urea

### Coating Process

- Coating Process
- Medtronic
DCB TECHNOLOGY
IN.PACT™ ADMIRAL™ DCB MECHANISM OF ACTION

Manufacturing:
- Balloon coated with matrix in semi-inflated state, then wrapped

During transit to lesion:
- Majority of matrix protected within folds of the balloon

DCB matrix coating:
- Paclitaxel + Urea

DCB inflation:
- Matrix contacts blood
- Blood hydrates urea
- Urea releases paclitaxel

Paclitaxel Hydrophobic and Lipophilic Properties:
- Facilitates transfer from balloon and stickiness to vessel wall
- Migrates through vessel wall deep into the media and adventitia
- Remains in vessel wall for over 180 days at therapeutic levels

1. Data on file at Medtronic (GLP Study F5208; GLP Study F5516)
Lutonix Formulation

Drug + Carrier = Coating

Drug
- Lutonix® 035 drug dose of Paclitaxel is 2μg/mm²

Carrier
- Polysorbate and Sorbitol

Coating
- Facilitates therapeutic drug retention and release of drug at the treatment site

Consistent Uniformity

Scientifically designed to deliver consistent coating, resulting in 360° paclitaxel treatment at the target vessel*

Uniform Delivery in vivo at 1 hour
(Animal vessel cross section after 30-sec. inflation*)
Design Summary of the FDA-Approved DCBs

Excipient is critical in delivering and sustaining paclitaxel in the tissue.

- Both devices use paclitaxel dosing significantly lower than other medical applications\(^1\)
- Excipient is unique to each DCB

<table>
<thead>
<tr>
<th>Drug (Dose)</th>
<th>Excipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel (3.5µg/mm(^2))</td>
<td>Urea</td>
</tr>
<tr>
<td>Paclitaxel (2.0µg/mm(^2))</td>
<td>Polysorbate-Sorbitol</td>
</tr>
</tbody>
</table>

\(^1\) Ng, Vivian. Eur J Clinical Investigation 2015;45(3):333-345
In.Pact SFA: Primary Patency 2 years

- **DCB**: 78.9%
- **PTA**: 50.1%

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**Number at risk**

<table>
<thead>
<tr>
<th></th>
<th>DCB</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>220</td>
<td>111</td>
</tr>
<tr>
<td>23</td>
<td>209</td>
<td>103</td>
</tr>
<tr>
<td>22</td>
<td>185</td>
<td>66</td>
</tr>
<tr>
<td>21</td>
<td>153</td>
<td>51</td>
</tr>
<tr>
<td>20</td>
<td>143</td>
<td>50</td>
</tr>
</tbody>
</table>
In.Pact SFA: Freedom CD-TLR 2 years

![Graph showing Freedom from CD-TLR for DCB and PTA]

- 91.0% for DCB
- 72.2% for PTA

Log-rank $P < 0.001$

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<thead>
<tr>
<th>Number at risk</th>
<th>Time after Index Procedure (Months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCB</td>
<td>220 211 200 179 167</td>
</tr>
<tr>
<td>PTA</td>
<td>111 106 88 77 76</td>
</tr>
</tbody>
</table>
IN.PACT SFA Trial: Primary Patency\(^1\) through 3 Years

1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 36 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment).

2. Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.
IN.PACT SFA Trial: Freedom from CD-TLR\(^1\) through 3 Years

Clinically-driven TLR adjudicated by an independent Clinical Events Committee, blinded to the assigned treatment based on any re-intervention at the target lesion due to symptoms or drop of ABI of ≥20% or >0.15 when compared to post-procedure baseline ABI.

1. Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.

\(^2\) Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.
Levant 2: Primary Patency 1 Year

Primary Patency (KM) at 365 Days

- Test DCB: 73.5%
- Control PTA: 56.8%

P = 0.001

Months from Randomization Date
Levant 2: Primary Patency 2 Year

Lutonix DCB Demonstrated Non-inferiority AND trend towards superiority versus PTA

<table>
<thead>
<tr>
<th>Composite Safety(^1)</th>
<th>Lutonix DCB (N=315)</th>
<th>Standard PTA (N=160)</th>
<th>Difference</th>
<th>Log-Rank P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>@730 days(^2)</td>
<td>78.7%</td>
<td>70.9%</td>
<td>7.8%</td>
<td>0.08</td>
</tr>
</tbody>
</table>
Role of Atherectomy
Is Atherectomy and Drug coated balloon all you need?
Not So Fast
Mechanism of Action

- Produces complete endothelial denudation in the dilated area with regrowth of the endothelial cells by 7 days
- Creates a tear that extended through the internal elastic lamina and into the media often followed by necrosis of the smooth muscle cells and damage to the normal architecture of the elastic fibers
- The tear or fracture of the intimal plaque and adjoining media is usually necessary for a successful procedure.
PTA: Utility...

- Small profile
- High pressure
- Caged / Constrained
- Scoring
- Cutting

Slide courtesy Dr. Bertolet
Self Expanding Stent
Stent Types

- Nitinol with ePTFE (Graft, interconnectors)
1 Year SFA Restenosis Rates

- PTA plus provisional stent
- Stent
- ASTRON
- ABSOLUTE
- RESILIENT
- FAST
- SCIROCCO
- FACT

Length of Lesion (cm) vs. Binary restenosis %
Restenosis: Achilles Heel
Complement
1. **PRE-DILATATION**
   - Required for all lesions prior to DCB procedure
   - Size - Diameter: 1 mm less than RVD
   - Size - Length: should not be greater than planned DCB length

2. **DRUG-COATED BALLOON**
   - DCB diameter RVD = 1:1; length 1 cm beyond lesion on both ends
   - Inflation: Time ≥ 3 minutes; Pressure < RBP as required to reach full DCB expansion
   - Overlap multiple DCBs by at least 1 cm

3. **POST-DILATATION**
   - If residual stenosis ≥ 50% or flow-limiting dissection
   - Standard or high pressure PTA balloon diameter 1:1 to RVD
   - Short/focal length as necessary to treat the extent of residual stenosis or dissection

4. **PROVISIONAL SPOT STENTING**
   - For persistent residual stenosis ≥ 50% or flow-limiting dissection
   - Minimum length as necessary to fully treat the residual stenosis or dissection
Drug Coated Balloon

*Primary Workhorse Therapy*

- PTA: Pre- & Post-Dilatation
- Stenting: Recoil, flow limiting dissection, residual stenosis
- Atherectomy: Debulking and severe calcification
Atherectomy, PTA and DCB
Atherectomy, PTA and DCB
Acknowledgements

Thank You
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