VEITH 2017

Current Status of all DCBs for Fem-Pop Lesions: RCTs and Other Evidence: Comparative Performance: All DCBs are not Equal

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Disclosure Statement of Financial Interest

• Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.
• Affiliation/Financial Relationship Company
  • Consulting Fees/Honoraria Boston Scientific, Medtronic, Abbott, Bard Peripheral Vascular
  • Research Support WL Gore
  • Scientific Advisory board/stock options Angiomed, Reflow Medical, Endoluminal Sciences, Syntervention, PO/Bypass, Shockwave Medical, Euroco Medical

Board Member: VIVA Physicians

DCB Landscape

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>DCB</th>
<th>Drug</th>
<th>Dose (μg/mm²)</th>
<th>Excipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medtronic</td>
<td>LUTONIX 035 (Bard)</td>
<td>Paclitaxel</td>
<td>2.0</td>
<td>Urea / Polysorbate</td>
</tr>
<tr>
<td>Spectranetics</td>
<td>IN.PACT Admiral (MDT)</td>
<td>Paclitaxel</td>
<td>3.5</td>
<td>Urea / Polysorbate</td>
</tr>
<tr>
<td>Adventis</td>
<td>STELLAREX PTX (Phillips)</td>
<td>Paclitaxel</td>
<td>2.0</td>
<td>Polyethylene Glycol</td>
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<tr>
<td>Lutonix</td>
<td>LUX (Bard)</td>
<td>Paclitaxel</td>
<td>2.0</td>
<td>Polyethylene Glycol</td>
</tr>
<tr>
<td>Passeo</td>
<td>LUX (Bard)</td>
<td>Paclitaxel</td>
<td>3.0</td>
<td>Butyryl-tri-hexyl Citrate</td>
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<tr>
<td>ADVANCE 18</td>
<td>LUX (Bard)</td>
<td>Paclitaxel</td>
<td>3.0</td>
<td>None</td>
</tr>
<tr>
<td>ELUTAX</td>
<td>PTX (Spectranetics)</td>
<td>Paclitaxel</td>
<td>2.2</td>
<td>Dextrane</td>
</tr>
<tr>
<td>FREEWAY PTX</td>
<td>PTX (Spectranetics)</td>
<td>Paclitaxel</td>
<td>3.0</td>
<td>Shellac</td>
</tr>
<tr>
<td>LEGFLOW PTX</td>
<td>PTX (Spectranetics)</td>
<td>Paclitaxel</td>
<td>3.0</td>
<td>Magnesium Stearate</td>
</tr>
<tr>
<td>RANGER PTX</td>
<td>PTX (Spectranetics)</td>
<td>Paclitaxel</td>
<td>2.0</td>
<td>Citrate Ester</td>
</tr>
<tr>
<td>LUMINOR PTX</td>
<td>PTX (Spectranetics)</td>
<td>Paclitaxel</td>
<td>3.0</td>
<td>Organic Ester</td>
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<td>sequent PTX</td>
<td>PTX (Spectranetics)</td>
<td>Paclitaxel</td>
<td>3.0</td>
<td>Iopromide</td>
</tr>
<tr>
<td>BIOPATH PTX</td>
<td>PTX (Spectranetics)</td>
<td>Paclitaxel</td>
<td>3.0</td>
<td>Shellac</td>
</tr>
</tbody>
</table>

13 DCBs in Europe

All DCBs Are Not Created Equal

Important Differences

• Dose (2.0 - 3.5 μg/mm²)
• Drug Formulation (crystalline vs. amorphous vs. hybrid)
• Excipient
• Balloon Surface Energies
• Coating Methods
• Usage methods (covering sheath, etc)
• Size matrix

DCB Device Overview

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<tr>
<th>Manufacturer</th>
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<th>Drug</th>
<th>Dose (μg/mm²)</th>
<th>Excipient / Coating</th>
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<td>IN.PACT</td>
<td>Admiral (MDT)</td>
<td>Paclitaxel</td>
<td>3.5</td>
<td>Urea / Polysorbate</td>
</tr>
<tr>
<td>Stellarex</td>
<td>(Phillips)</td>
<td>Paclitaxel</td>
<td>2.0</td>
<td>Polyethylene Glycol</td>
</tr>
</tbody>
</table>

Configurations:
- 4-7mm diameter 40-150mm length
- 4-7mm diameter 40-150mm length
- 4-120mm length

Platforms:
- Lutonix PTA
- Admiral PTA
- Stellarex PTA

Drug and Dosage:
- Paclitaxel 2.0μg/mm²
- Paclitaxel 3.5μg/mm²
- Paclitaxel 2.0μg/mm²

Excipient / Coating:
- Urea / Polysorbate
- Urea / Polysorbate
- Polyethylene Glycol

Commercial Availability:
- Worldwide
- Worldwide
- Worldwide

US Indication:
- ≤100mm lesions
- ≤150mm lesions
- ≤150mm lesions

What is the Evidence?

• IN.PACT Admiral (Medtronic)
  - Randomized Clinical Trials
  - IN.PACT SFA (331 patients)
  - IN.PACT Japan (100 patients)
  - Global Registry (1535 patients)
  - 3 imaging cohorts (in-stent restenosis, CTO, long lesion)
• Lutonix (Bard)
  - Randomized Clinical Trials
  - Levant 2 (476 patients)
  - Global Registry (691 patients)
• Stellarex (Phillips/Spectranetics)
  - Randomized Clinical Trials
  - ILLUMINATE EU (328 patients)
  - ILLUMINATE PIVOTAL (300 patients)
  - Global Registry (371 patients)
Caution When Comparing Data

- Differences in RCT design (Double blind vs. single blind, different lesion lengths, calcium, etc)
- Different core labs (ILLUMENATE)
- Different patency data (360 day vs. 390 day, KM analysis vs. discrete data, etc)
- Different scientific rigor of global registries (core lab vs. no core lab, phone call vs. office visit, adjudication of data, etc)

DCB Multicenter RCTs

Potentially different study-related variables
- Patient populations, lesion characteristics, study definitions, follow-up regimens, clinical events committees, core labs, etc.

Definitions
- Patency

Primary Patency of FDA-Approved DCBs

- IN.PACT ADMIRAL VS. LUTONIX
IN.PACT ADMIRAL VS. STELLAREX

2-year Primary Patency
ILLUMINATE EU RCT Study

Conclusions

- Good quality data available for the three FDA approved DCBs from well done randomized trials (with similar methodology)
- 2-year data from three of the trials demonstrates significant differences with regards to primary patency and freedom from TLR for at least one DCB – highlighting the fact that all DCBs are not created equal
- Many factors that may impact the efficacy of a DCB
- Further comparative studies required