Faculty Disclosure

Thomas Zeller, MD

For the 12 months preceding this presentation, I disclose the following types of financial relationships:

- **Honoraria received from:** Abbott Vascular, Angiomed, Bard Peripheral Vascular, Venray, Biotronik, Boston Scientific Corp., Cook Medical, Cordis Corp., Covidien, Gore & Associates, Medtronic, Spectranetics, Straub Medical, TriReme, VIVA Physicians
- **Consulted for:** Abbott Vascular, Bard Peripheral Vascular, Boston Scientific Corp., Cook Medical, Gore & Associates, Medtronic, Spectranetics, ReCar
- **Research, clinical trial, or drug study funds received from:** 480 biomedical, Bard Peripheral Vascular, Venray, Biotronik, Cook Medical, Cordis Corp., Covidien, Gore & Associates, Abbott Vascular - DEV Technologies, Inc., Medtronic, Spectranetics, Terumo, TriReme, Volcano

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**Trial Design INPACT SFA**

- **Pre-screening:**
  - Clinical and Anatomic Inclusion / Exclusion Criteria
- **Screening:**
  - Successful Pre-Dilatation
- **Randomization:**
  - IN.PACT (220) / PTA (111)
- **Secondary Analysis:**
  - (331 ITT ALL Subjects)
- **Primary Analysis:**
  - (301 ITT NON-Stented Subjects)

**Trial Design LEVANT 2**

- **Pre-Dilatation (n = 543)**
  - With Uncolored Balloons
- **Randomized 2:1**
- **Successful (n = 476)**
- **Suboptimal PTA (n = 67)**
  - Major Flow-Limiting Dissection OR >70% residual stenosis

**Levant 2: Blinding Steps Taken to Reduce Bias**

- **Blinded:**
  - Patient
  - Core Labs
  - DUS Tech
  - Evaluating physician
- **Not Blinded:**
  - Treating physician
  - Core Labs
  - DUS Tech
  - Evaluating physician

**Primary Objective and Endpoints**

**INPACT SFA**

- **Primary Efficacy Endpoint:**
  - Primary patency through 12 months, defined as freedom from clinically-driven TLR and DUS-derived restenosis (PSVR ≤ 2.4)
- **Primary Safety Endpoint:**
  - Freedom from device- and procedure-related death through 30 days, and freedom from target limb major amputation and clinically-driven TVR through 12 months

**LEVANT 2**

- **Primary Efficacy Endpoint:**
  - Primary patency of the target lesion at 1 YEAR in the absence of restenosis (defined by DUS PSVR ≤2.5 & freedom from target lesion revascularization (TLR))
- **Primary Safety Endpoint:**
  - Composite of freedom from all-cause peri-operative death & Freedom at 1 YEAR in the index limb from Amputation (above or below the ankle), TLR, and Index-limb-related death

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**Critical Analysis Of The LEVANT II And In.Pact SFA RCTs Of DEBs vs. POBA: What Are The Take Home Messages?**

Prof. Thomas Zeller
Department Angiology
University Heart-Center Freiburg - Bad Krozingen
Bad Krozingen, Germany

11/18/2015

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Baseline Angiographic 6 PROCEDURAL Characteristics
INPACT SFA vs. LEVANT 2

<table>
<thead>
<tr>
<th></th>
<th>IN.PACT DCB</th>
<th>PTA</th>
<th>Lutonix DCB</th>
<th>PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length (cm)</td>
<td>8.94 ± 4.89</td>
<td>8.81 ± 5.12</td>
<td>6.27±4.14</td>
<td>6.32±4.04</td>
</tr>
<tr>
<td>Total Occlusions (%)</td>
<td>25.8% (57)</td>
<td>19.5% (22)</td>
<td>20.6 (65)</td>
<td>21.9 (35)</td>
</tr>
<tr>
<td>Severe Calcification (%)</td>
<td>8.1% (18)</td>
<td>6.2% (7)</td>
<td>10.4 (33)</td>
<td>8.1 (13)</td>
</tr>
<tr>
<td>Diameter Stenosis pre (%)</td>
<td>81.1 ± 15.5</td>
<td>81.3 ± 13.7</td>
<td>80.5±14.8</td>
<td>80.9±14.9</td>
</tr>
<tr>
<td>Pre-dilatation (%)</td>
<td>96.4%</td>
<td>85.6%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Provisional Stenting (%)</td>
<td>7.3%</td>
<td>12.6%</td>
<td>2.5%</td>
<td>7.5%</td>
</tr>
</tbody>
</table>

12-month Effectiveness Outcomes (Primary Patency)
INPACT SFA vs. Levan 2

<table>
<thead>
<tr>
<th></th>
<th>IN.PACT DCB</th>
<th>PTA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Patency (PSVR ≤ 2.4)</td>
<td>82.2%</td>
<td>52.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lutonix DCB</td>
<td>Standard PTA</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Primary Patency (PSVR ≤ 2.4) @365 days</td>
<td>73.5%</td>
<td>56.8%</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Safety Outcomes
INPACT SFA & LEVANT 2

<table>
<thead>
<tr>
<th></th>
<th>IN.PACT DCB</th>
<th>PTA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Safety Composite</td>
<td>95.7% (198/207)</td>
<td>76.6% (82/107)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Composite Safety @365 days²</td>
<td>Lutonix DCB (N=316)</td>
<td>Standard PTA (N=160)</td>
<td>Difference</td>
</tr>
<tr>
<td></td>
<td>80.7%</td>
<td>81.5%</td>
<td>5.2%</td>
</tr>
</tbody>
</table>

Kaplan Meier Analysis - 12-month Primary Patency
INPACT SFA vs. LEVANT 2

ALL ITT, 12-month Clinically-driven TLR
INPACT SFA vs. LEVANT 2

<table>
<thead>
<tr>
<th></th>
<th>IN.PACT DCB</th>
<th>PTA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically-driven TLR</td>
<td>2.4%</td>
<td>20.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lutonix DCB</td>
<td>Standard PTA</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Clinically-driven TLR</td>
<td>10.3%</td>
<td>15%</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Functional Outcomes Trend in Favor of DCB

DCB patients required 88% less re-interventions to achieve the same level of function
Summary of 1-Year Secondary Clinical Endpoints

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Favor Control PTA</th>
<th>Favor IN.PACT DCB</th>
<th>Favor PTA</th>
<th>Favor IN.PACT DCB</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total TLR</td>
<td>75.7% (53/70)</td>
<td>89.3% (69/77)</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total TLR plus CEA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUS by PSVR &gt; 2.0</td>
<td>43.8% (14/32)</td>
<td>43.8% (14/32)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUS by PSVR &gt; 2.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DUS Clinical Patency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically-driven TLR</td>
<td>4.1% (3/74)</td>
<td>4.1% (3/74)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All TLR</td>
<td>25.7% (9/35)</td>
<td>25.7% (9/35)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2-Year Primary Patency

IN.PACT SFA vs. Levant 2

- Level 1 evidence for superior outcome of DCB vs. PTA at 12 months
- Similar patency outcomes for the control cohorts
- Differences in subgroup outcomes might be related to sample size

IN.PACT SFA vs. LUTONIX 2

- At 1-year:
  - Outcome regarding patency are now different favoring the IN.PACT technology
- A direct comparison between both DEB brands is needed for evaluation of performance differences