The importance of scientific evidence

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University Hospital Bern
Disclosure

Speaker name:

........I. Baumgartner.............................................................

I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- X Other(s) - educational grant COOK

I do not have any potential conflict of interest
More trials and technologies emerging each year.
Understanding strengths and shortcomings of each trial ... is more important and challenging than ever

Prof. M. Jaff
### 12-Month Primary Patency (K-M) for SFA Endovascular Therapies

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>cm</th>
<th>PSVR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PTA</strong></td>
<td>307</td>
<td>8.7</td>
<td>DUS</td>
</tr>
<tr>
<td>VIVA/Rocha-Singh (17)</td>
<td>134</td>
<td>6.1</td>
<td>2</td>
</tr>
<tr>
<td>Lifesent® RESILIENT (6)</td>
<td>250</td>
<td>7.7</td>
<td>2</td>
</tr>
<tr>
<td>S.M.A.R.T. Control® STROLL (6)</td>
<td>287</td>
<td>8.9</td>
<td>2</td>
</tr>
<tr>
<td>EverFlex™ DURABILITY II (7)</td>
<td>58</td>
<td>22</td>
<td>2.4</td>
</tr>
<tr>
<td>Lifesent® STELLA (8)</td>
<td>100</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>EverFlex™ DURABILITY 200 (9)</td>
<td>72</td>
<td>19</td>
<td>2.4</td>
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<tr>
<td>Viabahn® VIABAHN 25 cm (11)</td>
<td>71</td>
<td>26</td>
<td>2.5</td>
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<tr>
<td>Covered</td>
<td>787</td>
<td>9.9</td>
<td>NA</td>
</tr>
<tr>
<td>DES</td>
<td>241</td>
<td>5.5</td>
<td>2</td>
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<tr>
<td>Supera</td>
<td>264</td>
<td>7.8</td>
<td>2.4</td>
</tr>
<tr>
<td>Atherectomy</td>
<td>495</td>
<td>12.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Spectranetics CELLO (16)</td>
<td>253</td>
<td>8.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Diamondback 360® COMPARE 360 (13)</td>
<td>38</td>
<td>6.8</td>
<td>2.4</td>
</tr>
<tr>
<td>TurboHawk™ DEFINITIVE LE (12)</td>
<td>232</td>
<td>14.6</td>
<td>2.4</td>
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<tr>
<td>Pathway PVD Trial (15)</td>
<td>172</td>
<td>2.7</td>
<td>2.4</td>
</tr>
<tr>
<td>Spectranetics CELLO (16)</td>
<td>65</td>
<td>5.6</td>
<td>DUS</td>
</tr>
</tbody>
</table>
Primary Patency Rates

- PTA (optimal/suboptimal)
- PTA plus provisional stent
- Primary Stent
- DES

Binary restenosis @ 12 months (%)

Length of the lesion (cm)
<table>
<thead>
<tr>
<th>Study Parameters</th>
<th>Zilver PTX: Zilver Global (SAS)</th>
<th>Supera Superb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study size</td>
<td>N=787</td>
<td>N=264</td>
</tr>
<tr>
<td>PSV ratio</td>
<td>&lt;2.0</td>
<td>&lt;2.0</td>
</tr>
<tr>
<td>Pre-dil required?</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>Rutherford I/E</td>
<td>2-6</td>
<td>2-4</td>
</tr>
<tr>
<td>L%DS</td>
<td>85%</td>
<td>78%</td>
</tr>
<tr>
<td>CTOs</td>
<td>38%</td>
<td>25%</td>
</tr>
<tr>
<td>In-stent restenosis*</td>
<td>15%</td>
<td>0%</td>
</tr>
<tr>
<td>Mod-severe calcified</td>
<td>72%</td>
<td>73%</td>
</tr>
<tr>
<td>Mean lesion length</td>
<td>100mm</td>
<td>83mm</td>
</tr>
<tr>
<td>1-yr TLR</td>
<td>10%</td>
<td>11%</td>
</tr>
<tr>
<td>2-yr TLR</td>
<td>13%</td>
<td>17%</td>
</tr>
<tr>
<td>1-yr primary patency</td>
<td>83%</td>
<td>86%</td>
</tr>
</tbody>
</table>
Zilver PTX RCT Study Design

Enrollment

Primary Randomization

PTA

Zilver PTX

Suboptimal PTA

Optimal PTA

Secondary Randomization

Provisional BMS

Provisional Zilver PTX
12-Month Primary Patency (K-M) for SFA Endovascular Therapies

- PTA: 33%
- Standard Nitinol Stents: 81%, 80%, 77%, 66%, 65%
- Covered: 71%, 67%
- DES: 83%, 90%
- Supera: 86%, 83%
- Atherectomy: 75%, 75%, 65%

**n**
- 307
- 134
- 250
- 287
- 58
- 100
- 72
- 71
- 787
- 61
- 264
- 495
- 253
- 38
- 232

**cm**
- 8.7
- 6.1
- 7.7
- 8.9
- 22
- 24
- 19
- 26
- 9.9
- 5.5
- 7.8
- 12.6
- 8.1
- 6.8
- 14.6

**PSVR**
- DUS: 2.5
- 2
- 2
- 2.4
- 2.4
- 2.4
- NA
- 2
- 2
- 2
- 2
- 2.4
- 2.4
- 2.5
- 2.4
78.9% Primary patency at 2 years
Highest reported patency of available SFA technologies

Primary Patency: SFA Pivotal Trials

- IN.PACT SFA² IN.PACT™ Admiral™ DCB
  - Primary Patency: 78.9%
  - Lesion Length: 8.9 cm

- LEVANT 2² Lutonix™ DCB
  - Primary Patency: 58.6%
  - Lesion Length: 6.3 cm

- Zilver PTX RCT³ Zilver PTX™ DES
  - Primary Patency: 74.8%
  - Lesion Length: 6.6 cm

- STROLL⁴ Smart Stent™ BMS
  - Primary Patency: 74.9%
  - Lesion Length: 7.7 cm

- RESILIENT⁵ LifeStent™ BMS
  - Not reported
Why you can’t compare trials: Trial Design

Zilver PTX Randomized Trial

DCB Trial Designs

Included in ZPTX Trial

Excluded in DCB Trials
IN.PACT SFA (In.Pact)
331-Patient, multicenter Randomized Trial

Primary Patency Results through 2 Years

- DCB: 78.9%
- PTA: 50.1%

Log-rank $P < 0.001$

Primary Patency defined as freedom from clinically driven TLR and restenosis as determined by a duplex ultrasonography derived PSVR of ≤2.4

1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) or clinically-driven target lesion revascularization through 24 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 the 30-day window prior to each follow-up interval

J.Laird et al. Sustained Durability of Treatment Effect Using a Drug-Coated Balloon for Femoropopliteal Lesions: 24-Month Results of IN.PACT SFA J Am Coll Cardiol. 2015
LEVANT 2 (Lutonix)
476-Patient, multicenter Randomized Trial

Primary patency defined as absence of restenosis (defined by DUS PSVR ≥2.5) & freedom from TLR

- K.Rosenfield TCT 2014 oral presentation
- SVS 2015
Primary Patency Rates: DCB Angioplasty

Efficacy results with different DCB are not uniform: no class effect.
Why you can’t compare trials: PSVR threshold

<table>
<thead>
<tr>
<th></th>
<th>Zilver PTX</th>
<th>Supera 500</th>
<th>In.Pact Admiral</th>
<th>Lutonix</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSVR</td>
<td>2.0</td>
<td>2.4</td>
<td>2.4</td>
<td>2.5</td>
</tr>
</tbody>
</table>

PSVR ≥ 2.0
(≥40\% stenosis)

PSVR ≥ 2.5
(≥50\% stenosis)

Why you can’t compare trials: PSVR threshold

Secondary Effectiveness Endpoints
12-Month Patency – PSVR Levels

<table>
<thead>
<tr>
<th>Threshold for Binary Restenosis (primary analysis)</th>
<th>Test DCB</th>
<th>Control PTA</th>
<th>Difference % [95% CI]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Core Lab Adjudications</td>
<td>64.0%</td>
<td>53.2%</td>
<td>12.6%</td>
<td>0.015</td>
</tr>
<tr>
<td>DUS PSVR ≥ 2.5 (per original protocol)</td>
<td></td>
<td></td>
<td>12.9%</td>
<td>0.017</td>
</tr>
<tr>
<td>DUS PSVR ≥ 2.0</td>
<td></td>
<td></td>
<td>8.2%</td>
<td>0.130</td>
</tr>
</tbody>
</table>

11% DROP IN PATENCY!

Patency endpoint significant at PSVR of 2.5 and 3.0. Patency endpoint not significant at PSVR 2.0.
Why you can’t compare trials: PSVR threshold

NO DIFFERENCE BETWEEN POBA AND DCB!

Patency endpoint significant at PSVR of 2.5 and 3.0.
Patency endpoint not significant at PSVR 2.0.
So, if we don’t compare trials, what’s the basis for device selection?

Two things:
1. Long-term performance in RCTs (Level 1 data).
2. Consistent performance across multiple trials.
Conclusion

• Comparing patency and freedom from TLR from different trials is misleading and bad science
  – Different trial designs
  – Different definitions of patency
  – Different patients and lesions

• Long-term, level I RCT evidence as well as consistent results across “real-world” registries are needed to aid in clinical decision making
The importance of scientific evidence

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