Are drug-eluting devices the new standard for femoropopliteal interventions in claudication?

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Disclosure

Peter A. Schneider

I have the following potential conflicts of interest to report:

Scientific Advisory Board (non-paid): Cardinal, Abbott, Medtronic

Royalty (modest): Cook

Co-founder and Chief Medical Officer: Intact, Cagent

Enter patients into studies: NIH, Bard, Gore, Medtronic, BSI, Silk Road (no financial relationship).

VIVA Board member (nonprofit)
Timing of SFA restenosis is longer compared to coronary stenting, which predominantly occurs within 6 months after stenting.

Factors for restenosis in the SFA include the number of runoff vessels, severity of lower limb ischemia, and length of diseased segments.

Femoral-popliteal Technology

Work in Progress

RCT Data: PTA vs Stent

- PTA
- DES

Lesion length (cm)

12-month Primary Patency

- Stents
- PTA

RCTs
- Resilient
- FACT
- 4EVER
- Durability
- Astron
- Zilver PTX
- Vienna
- Vienna-3
Femoral-popliteal Technology

Work in Progress

RCT Data: PTA, stent, DES, stent-graft

12-month Primary Patency

Lesion length (cm)

Stent-graft RCTs
Viper
Vibrant
Viastar
SUSTAINED DRUG, SUSTAINED BENEFIT.

IMPORTANCE OF DRUG "RESERVOIRS"

PACLITAXEL RESERVOIR

Solid-phase paclitaxel embeds in the vessel wall, creating "reservoirs" that provide sustained release of drug over time.

From R Vermani, Charing Cross 2016
Levant Study
12-month Primary Patency

IN.PACT SFA
12-month Primary Patency

Lesion length 8.9cm

Randomized Control Trials
DCB vs PTA

Lesion length 6.3cm
Treated length 10.8cm

Proportions-based difference was 65.2% for DCB vs. 52.6% for standard PTA → 12.6% difference
Femoral-popliteal Technology
Work in Progress

RCT Data: DCB
No implant!

12-month Primary Patency vs. Lesion length (cm)
IN.PACT SFA Trial 3-year Primary Patency Benefit is Sustained

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.
Primary Patency-DCB Long Lesions

Lesions >15cm (TASC C&D only)
Mean lesion length 25cm
49.5% occlusions
Primary patency at 1 year = 83.2%

Micari et al. JACC Cardiovasc Interv 2016;9;950
Lesions >15cm (TASC C&D only)
Mean lesion length 24cm
65.3% occlusions
Primary patency:
1 year = 79.2%
2 years = 53.7%
IN.PACT Global (>1500 patients)

**Provisional Stent**

<table>
<thead>
<tr>
<th>Length</th>
<th>Percentage</th>
<th>N</th>
<th>Mean Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>LL 15-25 cm</td>
<td>40.4%</td>
<td>156</td>
<td>26.4 cm</td>
</tr>
<tr>
<td>LL &gt; 25 cm</td>
<td>33.3%</td>
<td>99</td>
<td>23.0 cm</td>
</tr>
<tr>
<td>LL &gt; 25 cm</td>
<td>52.6%</td>
<td>57</td>
<td>26.3 cm</td>
</tr>
</tbody>
</table>

N=157
Mean length 26.4 cm

N=126
Mean occlusion length 22.9 cm

**Occlusions**

46.8% (59/126)
Zilver: DES vs BMS 5-year Patency Benefit is Sustained

Zilver PTX 72.4%

BMS 53.0%

$p = 0.03$

<table>
<thead>
<tr>
<th>Years (LESIONS)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Provisional Zilver PTX</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At Risk</td>
<td>63</td>
<td>55</td>
<td>46</td>
<td>38</td>
<td>31</td>
<td>25</td>
</tr>
<tr>
<td>Failed</td>
<td>0</td>
<td>6</td>
<td>10</td>
<td>11</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td><strong>Provisional BMS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At Risk</td>
<td>62</td>
<td>42</td>
<td>35</td>
<td>29</td>
<td>26</td>
<td>19</td>
</tr>
<tr>
<td>Failed</td>
<td>0</td>
<td>15</td>
<td>20</td>
<td>23</td>
<td>24</td>
<td>26</td>
</tr>
</tbody>
</table>
Zilverpass Trial: Zilver PTX versus above-knee fem-pop

Mean lesion length: 25cm

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>30 days</th>
<th>6MFU</th>
<th>12MFU</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ZILVER PTX</strong></td>
<td>Tar</td>
<td>57</td>
<td>52</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>100</td>
<td>100</td>
<td>97.9</td>
</tr>
<tr>
<td><strong>BYPASS</strong></td>
<td>Tar</td>
<td>57</td>
<td>51</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>100</td>
<td>96.3</td>
<td>80.9</td>
</tr>
</tbody>
</table>

P = 0.550
Primary Patency
DCB vs DES for Long Lesions

Lesions >10cm
Mean lesion length 19cm
53% occlusions
Primary patency at 1 year:
DCB = 76.1%
DES = 69.6%

Zeller et al. J Endovasc Ther 2014;21;359
# Drug Eluting Stent

Zilver for Femoral-popliteal Disease

<table>
<thead>
<tr>
<th>Reference</th>
<th>n</th>
<th>Lesion length</th>
<th>Primary patency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosiers et al. J Cardiovasc Surg 2013;54:115</td>
<td>787</td>
<td>22.6 cm</td>
<td>77.6%</td>
</tr>
<tr>
<td>Devaine et al. Eur J Vasc Endovasc Surg 2015;50:631</td>
<td>45 (Incl. ISR, CLI, concomitant procedures 47%)</td>
<td>25.2</td>
<td>52.5%</td>
</tr>
<tr>
<td>Zilverpass RCT</td>
<td>57</td>
<td>25.0</td>
<td>78.1%</td>
</tr>
</tbody>
</table>
Drug release from the Eluvia system is sustained over time

>90% of drug is released at 1 year

Drug release coincides with highest risk period for restenosis

Based on pre-clinical PK analysis. Data on file at Boston Scientific.


Eluvia is an investigational device. Limited under U.S. law for investigational use only. Not available for sale.
# SFA DES: IMPERIAL Trial

## Clinical Study Overview

<table>
<thead>
<tr>
<th>Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>465 subjects treated with ELUVIA (N=310) or Zilver PTX (N=155)</td>
</tr>
<tr>
<td>First patient enrolled December, 2015</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Investigational Centers</th>
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<tbody>
<tr>
<td>Up to 75 study centers worldwide:</td>
</tr>
<tr>
<td>US, Canada, New Zealand, Belgium, Germany, Austria, and Japan</td>
</tr>
<tr>
<td>Up to 10 study centers in US will enroll subjects in the PK substudy</td>
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</tbody>
</table>

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<thead>
<tr>
<th>Primary Efficacy Endpoint</th>
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</thead>
<tbody>
<tr>
<td>Primary vessel patency as assessed by duplex ultrasound (DUS) at 12 months post-procedure and adjudicated by an independent core laboratory.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Primary Safety Endpoint</th>
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</thead>
<tbody>
<tr>
<td>Major Adverse Event (MAE) rate defined as</td>
</tr>
<tr>
<td>All cause death through 1 month</td>
</tr>
<tr>
<td>Target limb major amputation through 12 months</td>
</tr>
<tr>
<td>Target lesion revascularization (TLR) through 12 months</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study Design</th>
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</thead>
<tbody>
<tr>
<td>The trial consists of the following:</td>
</tr>
<tr>
<td>A prospective, multicenter, 2:1 randomized (ELUVIA vs Zilver PTX), controlled, single-blind, non-inferiority trial (RCT)</td>
</tr>
<tr>
<td>A concurrent, non-blinded, non-randomized, single-arm, pharmacokinetic (PK) substudy</td>
</tr>
<tr>
<td>A subject may be enrolled in the RCT or the substudy; but not in both</td>
</tr>
</tbody>
</table>
SFA DES trials

Improving results with SFA DES

Müller-Hülsbeck, S. Presented at VIVA 2015
Dake et al. J Endovasc Ther 2011
Duda et al. J Endovasc Ther 2006
Femoral-popliteal Technology

Work in Progress

Lesion length (cm)

12-month Primary Patency

- PTA
- Stent
- Stent-graft
- DES
- DCB
- Atherectomy

DCB/DES for TASC C/D

Registries
IN.PACT Global Leipzig Bad Krozingen Italy Definitive LE Superb Zilverpass Zilver Registry
Conclusion
Drug Eluting Devices Are the New Standard

• Drug coated balloons and drug eluting stents provide patency rates in the femoral-popliteal segment that is superior to what could previously been achieved.

• Although development will continue in this area, drug eluting devices appear to be a new standard for femoral-popliteal intervention.
Are drug-eluting devices the new standard for femoropopliteal interventions in claudication?

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