Is There a Durable Treatment Option for Challenging Lesions? The Scientific Evidence for Drug-Coated Balloons

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Disclosure

Speaker name: Andrew Holden, MBChB, FRANZCR

I have the following potential conflicts of interest to report:

- [x] Consulting – Scientific Advisory Board Member, MEDTRONIC
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest
IN.PACT SFA Trial

1 Year

2 Year

Peripheral Vascular Disease
Treatment Effect of Drug-Coated Balloons Is Durable to 3 Years in the Femoropopliteal Arteries
Long-Term Results of the IN.PACT SFA Randomized Trial
Peter A. Schneider, MD, John R. Laird, MD, Gunnar Tepe, MD, Mariame Belhassen, MD, Thomas Zeller, MD, Dirk Schneiber, MD, Christopher Morgan, MD, Antonio Malas, MD, Erich Sach, MD, Michael E. Jeff, DO, Hong Wang, MD, PhD, Melissa S. Rhee, PhD, Prakash Kirthali, MD, for the IN.PACT SFA Trial Investigators

3 Year

4 Year
Presented by Schneider P. VIVA 2017.

Longest Term Data Published

5 Year

Drug-Coated Balloon Versus Standard Percutaneous Transluminal Angioplasty for the Treatment of Superficial Femoral and Popliteal Peripheral Artery Disease: 12-Month Results from the IN.PACT SFA Randomized Trial
Gunnar Tepe, MD, John Laird, MD, Peter Schneider, MD, Mariame Belhassen, MD, Prakash Kirthali, MD, Antonio Malas, MD, Christopher Morgan, MD, Dirk Schneiber, MD, Thomas Zeller, MD, David L. Cohen, MD, PhD, David D. Shaw, MD, Blake Alexander, MD, and Marie Latar-N, MD, Michael J. Jeff, DO, for the IN.PACT SFA Trial Investigators

Drug-Coated Balloons Show Superior 4-Year Outcomes versus Angioplasty: Results from the IN.PACT SFA Randomized Trial
Peter Schneider, MD, Kaiser Permanente Hospital, Norwalk, CA, Presented as part of the IN.PACT SFA Trial.
IN.PACT SFA Trial
Overview

Robust Level 1 Evidence
- Prospective, two-phase, multicenter (EU and US), Randomized (2:1), single-blinded (subjects, sponsor trial management)

Rigorous and Unbiased
- Independent and blinded Duplex Ultrasound Core Lab\(^1\), Angiographic Core Lab\(^2\), and Clinical Events Committee\(^3\)
- Independent Data Safety Monitoring Board\(^3\)
- External monitoring with 100% source data verification

Durability of Outcomes
- Subjects followed up to 5 years

1-Year Results

2-Year Results

3-Year Results

5-Year Results

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1. VasCore DUS Core Laboratory, Boston, MA, US.
2. SynvaCor Angiographic Core Laboratory, Springfield, IL, US.
3. Clinical Events Committee and Data Safety Monitoring services provided by HCRI, Boston, MA, US.
IN.PACT SFA Trial
Freedom from CD-TLR Through 5 Years

Log-rank $P = 0.0196$

Number at risk

Time After Index Procedure (Months)

Statistically Significant

1. Laird et al. CIRC CI. 2019;12:e007702
IN.PACT SFA Trial
Freedom from CD-TLR Through 5 Years

CD-TLR Rates

1. Laird et al. CIRC CI. 2019;12:e007702
### IN.PACT SFA Trial

#### 5-Year Outcomes

### Additional Effectiveness Outcomes

<table>
<thead>
<tr>
<th>5-Year Outcome</th>
<th>IN.PACT Admiral (n = 220)</th>
<th>DCB (n = 111)</th>
<th>PTA (n = 111)</th>
<th>P-value¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically-driven TLR²</td>
<td>25.5% (47/184)</td>
<td>35.6% (37/104)</td>
<td>0.080</td>
<td></td>
</tr>
<tr>
<td>All TLR³</td>
<td>26.6% (49/184)</td>
<td>37.5% (39/104)</td>
<td>0.063</td>
<td></td>
</tr>
</tbody>
</table>

1. Unless otherwise indicated, all tests were for superiority using the Fisher’s exact test for binary variables and t-test for continuous variables.
2. Clinically-driven TLR adjudicated by an independent Clinical Event 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.
3. Any TLR includes clinically-driven and incidental or duplex driven TLR.

### Days to First CD-TLR (mean ± SD)

- **PTA**: 474.9 ± 484.3 days
- **DCB**: 807.5 ± 433.9 days

P < 0.001
## IN.PACT SFA Trial: 5-Year
Hazard Ratio for CD-TLR by Subgroups (DCB v PTA)

**DCB favored in subgroups that are risk factors for restenosis**
- RCC 4
- Age >75
- Longer and Occluded lesions
- Females

### Subgroup Analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>IN.PACT DCB %</th>
<th>Control PTA %</th>
<th>Hazard Ratio [95% CI]</th>
<th>p-value</th>
<th>p-value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall ITT</td>
<td>74.5%</td>
<td>66.3%</td>
<td>0.60 [0.39, 0.93]</td>
<td>0.021</td>
<td>0.190</td>
</tr>
<tr>
<td><strong>Rutherford Classification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 2</td>
<td>72.4%</td>
<td>68.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 3</td>
<td>76.3%</td>
<td>67.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Category 4</strong></td>
<td>68.2%</td>
<td>16.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>70.3%</td>
<td>64.4%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>77.1%</td>
<td>66.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;= 75</td>
<td>90.6%</td>
<td>66.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 75</td>
<td>69.4%</td>
<td>65.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lesion Length</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 cm</td>
<td>79.9%</td>
<td>69.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;=5 cm and &lt;10 cm</td>
<td>71.6%</td>
<td>68.5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;=10 cm and &lt;18 cm</td>
<td>75.1%</td>
<td>60.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Occlusion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>75.4%</td>
<td>51.9%</td>
<td></td>
<td>0.394</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>74.0%</td>
<td>68.4%</td>
<td></td>
<td>0.038</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>67.4%</td>
<td>52.9%</td>
<td></td>
<td>0.156</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>78.2%</td>
<td>71.1%</td>
<td></td>
<td>0.016</td>
<td></td>
</tr>
</tbody>
</table>

IN.PACT SFA Trial: Diabetic Status
Freedom from CD-TLR Through 5 Years

1. Laird et al. CIRC CI. 2019;12:e007702
IN.PACT Japan Trial
Overview

Objective: Assess the safety and effectiveness of MDT-2113 (IN.PACT Admiral) DCB for the interventional treatment of de novo and non-stented restenotic lesions in the superficial femoral artery and the proximal popliteal artery as compared to treatment with standard percutaneous transluminal angioplasty

- Prospective, multi-center, randomized (2:1), single blinded trial*
- 100 subjects enrolled at 11 sites in Japan
  - MDT-2113 DCB (n=68) vs. PTA (n=32)
- Independent and blinded Duplex Ultrasound Core Lab,[1] Angiographic Core Lab,[2] and Clinical Events Committee[3]
- External Monitoring, 100% Source Data Verification

* Sponsored by Medtronic plc
1. VasCore DUS Core Laboratory, Boston, MA, US;
2. SynvaCor Angiographic Core Laboratory, Springfield, IL, US;
3. Clinical Events Committee and Data Safety Monitoring services provided by HCRI, Boston, MA, US
IN.PACT Japan Trial
Outcomes Through 3 Years

**Primary Patency**

- Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) and clinically-driven target lesion revascularization through 24 months (adjudicated by a Clinical Events Committee blinded to the assigned treatment)

- Number at risk represents the number of evaluable subjects at the beginning of the 30-day window prior to each follow-up interval

**Freedom from CD-TLR**

- Log-rank $p = 0.001$
- Log-rank $p = 0.451$

1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) and 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
### IN.PACT Japan Trial
#### Safety Outcomes Through 3 Years

<table>
<thead>
<tr>
<th>Event</th>
<th>MDT-2113 DCB (N=68 Subjects)</th>
<th>PTA (N=32 Subjects)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Safety Composite</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>83.6% (56/67)</td>
<td>75.9% (22/29)</td>
<td>0.402</td>
</tr>
<tr>
<td><strong>30-day Device- &amp; Proc.-related Death</strong></td>
<td>0.0% (0/68)</td>
<td>0.0% (0/32)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td><strong>36-month Major Adverse Event</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>20.9% (14/67)</td>
<td>31.0% (9/29)</td>
<td>0.306</td>
</tr>
<tr>
<td><strong>36-month Target Limb Major Amputation</strong></td>
<td>0.0% (0/67)</td>
<td>0.0% (0/29)</td>
<td>&gt; 0.999</td>
</tr>
<tr>
<td><strong>36-month Clinically Driven TVR</strong></td>
<td>16.4% (11/67)</td>
<td>24.1% (7/29)</td>
<td>0.402</td>
</tr>
<tr>
<td><strong>All-cause Death</strong></td>
<td>6.0% (4/67)</td>
<td>6.9% (2/29)</td>
<td>1.000</td>
</tr>
<tr>
<td><strong>Thrombosis</strong></td>
<td>1.5% (1/67)</td>
<td>0.0% (0/29)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

1. Primary safety composite is defined as freedom from device- and procedure-related 30-day death and freedom from target limb major amputation and clinically-driven TVR through 24 months.
2. MAE is defined as composite of death, clinically-driven TVR, target limb major amputation, and thrombosis within 24 months.
Pooled IN.PACT SFA and Japan RCTs
Dose Not Correlated to Mortality Through 5 Years

Mortality by Dose Tercile

<table>
<thead>
<tr>
<th>Cumulative Incidence (cumulative deaths)</th>
<th>Time After Index Procedure (Years)</th>
<th>HR (DCB vs PTA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA</td>
<td>0.0% (0)</td>
<td></td>
</tr>
<tr>
<td>DCB Lower Tercile</td>
<td>0.0% (0)</td>
<td></td>
</tr>
<tr>
<td>DCB Mid Tercile</td>
<td>0.0% (0)</td>
<td></td>
</tr>
<tr>
<td>DCB Upper Tercile</td>
<td>0.0% (0)</td>
<td></td>
</tr>
</tbody>
</table>

- **15.7%** DCB Lower tercile 4.0 mg*
- **14.8%** DCB Mid tercile 7.3 mg*
- **13.4%** DCB Upper tercile 12.3 mg*
- **12.0%** PTA

*Presented by Mauri L, Circulatory System Devices Panel Meeting, Gaithersburg, MD June 19, 2019

**p-value 0.73**
Summary

• The IN.PACT™ Admiral™ Clinical Program remains the largest, independently adjudicated cohort treated with DCB for femoropopliteal disease
• Results from the IN.PACT RCT trials (IDE and Japan) demonstrate;
  • Long-term effectiveness and safety
  • No relationship between Paclitaxel Dose and Mortality Rate
Is There a Durable Treatment Option for Challenging Lesions? The Scientific Evidence for Drug-Coated Balloons

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