Clinical evidence of IN.PACT and opportunities of DAART for the treatment of PAD

Michel Bosiers MD
Vascular and endovascular surgeon
St- Franziskus-Hospital Münster, Germany
Director: Prof. G. Torsello
Disclosure

Speaker name:
....Michel Bosiers........................................................

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☒ I do not have any potential conflict of interest
Background

- Endovascular approach first-line therapy for PAD management
- No single device modality “gold standard”
- DCBs: improved outcomes over PTA at 1 and 2 years in randomized trials
- IN.PACT DCB benefit through 5 years?
- Adequate vessel preparation for optimal DCB effect
- Evidence points to the use of Atherectomy followed by DCB for improved outcomes
IN.PACT Admiral Clinical Program

RCTs + Approval Studies
- IN.PACT SFA (EU+US) RCT¹
- IN.PACT JAPAN RCT¹
- IN.PACT China¹
  - Gender Subset
    - Diabetic Subset

Real-World Study
- IN.PACT Global Study²
  - Pre-specified Imaging Cohorts
    - Long Lesion¹
    - ISR¹
    - CTO¹
  - Regional Subset
    - Belgian
    - ASEAN

A robust catalog of 1837 patients across multiple studies

1. Core lab-adjudicated with clinical events committee oversight.
2. Clinical events committee oversight.
The only long-term data of any commercially-available DCB

4-Year Results: Presented by P. Schneider VIVA 2017
5-Year Results: Presented by J. Laird VIVA 2018
1. Core lab adjudicated with clinical events committee oversight.
2. Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.
3. Clinically-driven TLR adjudicated by an independent Clinical Events 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.

The only long-term data of any commercially-available DCB

4-Year Results: Presented by P. Schneider VIVA 2017
5-Year Results: Presented by J. Laird VIVA 2018
IN.PACT Admiral Clinical Program

RCTs + Approval Studies
- IN.PACT SFA (EU+US) RCT
  - Gender Subset
    - Diabetic Subset
- IN.PACT JAPAN RCT
- IN.PACT China

Real-World Study
- IN.PACT Global Study
  - Pre-specified Imaging Cohorts
    - Long Lesion
    - ISR
    - CTO
  - Regional Subset
    - Belgian
    - ASEAN

A robust catalog of 1837 patients across multiple studies

1. Core lab-adjudicated with clinical events committee oversight.
2. Clinical events committee oversight.
IN.PACT Global: 3-year Results

1. Core lab-adjudicated with clinical events committee oversight.
2. Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.
3. Clinically-driven TLR adjudicated by an independent Clinical Events 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.

4-Year Results: Presented by P. Schneider VIVA 2017
5-Year Results: Presented by J. Laird VIVA 2018

Largest real-world study of DCB with independent clinical events committee and core-lab adjudication of outcomes
Long and Complex lesions drawn from IN.PACT Global imaging cohorts

Subjects enrolled in IN.PACT Global imaging cohorts with single lesions >18cm were retrospectively analyzed - 12-mo primary patency - 12-mo safety composite endpoints

1. Core lab-adjudicated with clinical events committee oversight.  
2. Clinical events committee oversight.
Subjects enrolled in IN.PACT Global imaging cohorts with single lesions >18cm were retrospectively analyzed.

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>IN.PACT™ Admiral™ DCB n = 227 subjects and Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, ± SD</td>
<td>68.8 ± 9.7</td>
</tr>
<tr>
<td>Male Gender</td>
<td>67.4% (153/227)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>85.7% (197/230)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>71.7% (157/219)</td>
</tr>
<tr>
<td>ABI / TBI, ± SD†</td>
<td>0.625 ± 0.214</td>
</tr>
<tr>
<td>Lesion Length, ± SD</td>
<td>28.74 ± 7.11</td>
</tr>
<tr>
<td>Total Occlusions</td>
<td>70.1% (157/224)</td>
</tr>
</tbody>
</table>

† ABI for all target limbs treated during the 1st index procedure are included (can be bilateral).
‡ Dattilo R, et al. J Invasive Cardiol 2014;26:355-360. Severe calcium definition used by study sites and core laboratory as bilateral calcium at the same location (also measured in sections), ≥ half of the total lesion length, ≥180° (both sides of the vessel at the same location).
* All ITT subjects (stented and non-stented)
1. All ITT subjects (stented and non-stented)
2. Device success defined as successful delivery, inflation, deflation and retrieval of the intact study balloon device without burst below the RBP.
3. Procedure success defined as residual stenosis of ≤ 50% (non-stented subjects) or ≤ 30% (stented subjects) by core lab (if core lab was not available then the site-reported estimate was used).
4. Clinical success defined as procedural success without procedural complications (death, major target limb amputation, thrombosis of the target lesion, or TVR) prior to discharge.

## Procedural Characteristics

### IN.PACT™ Admiral™ DCB

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-dilatation (%)</td>
<td>89.0% (202/227)</td>
</tr>
<tr>
<td>Post-dilatation (%)</td>
<td>44.7% (101/226)</td>
</tr>
<tr>
<td>Dissections (%)</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>36.1% (82/227)</td>
</tr>
<tr>
<td>A-C</td>
<td>35.6% (81/227)</td>
</tr>
<tr>
<td>D-F</td>
<td>19.3% (44/227)</td>
</tr>
<tr>
<td>Provisional Stenting (%)</td>
<td>42.5% (96/226)</td>
</tr>
<tr>
<td>Device Success (%)</td>
<td>99.2% (653/658)</td>
</tr>
<tr>
<td>Procedural Success (%)</td>
<td>99.1% (224/226)</td>
</tr>
<tr>
<td>Clinical Success (%)</td>
<td>99.1% (224/226)</td>
</tr>
</tbody>
</table>
Primary Patency through 12-Months

1. Freedom from core laboratory-assessed restenosis (duplex ultrasound PSVR ≤2.4) and 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 60-day window.

Number at risk: 227

Day 360: 89.1%

Day 420: 77.1%

The only DCB to show remarkable effectiveness in long lesions with mean length of 28.74 cm
1. Clinically-driven TLR adjudicated by an independent Clinical Events 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.
2. Number at risk represents the number of evaluable subjects at the beginning of each 30-day window.
Technical challenges remain for optimal PAD treatment

Primary patency is high in DCB trials but provisional stent rate increases with increasing lesion length.

Standard angioplasty can result in overstretch and mechanical recoil.

Calcium may act as a barrier to drug uptake.

Looking beyond POBA for vessel prep to overcome these challenges

Balloons
- Cutting Balloons
- Scoring Balloons
- Controlled-inflation Balloon

Atherectomy Devices
- Directional
- Orbital
- Rotational
- Laser
- Hybrid
## Definitive LE Trial – Baseline and Outcomes

### Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Claudicant n = 598</th>
<th>CLI n = 201</th>
<th>P value</th>
<th>All Patients n = 799</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Lesions</td>
<td>743</td>
<td>279</td>
<td>n/a</td>
<td>1022</td>
</tr>
<tr>
<td>Mean Length (cm ± SD)</td>
<td>7.5 ± 5.3</td>
<td>7.2 ± 5.5</td>
<td>0.381</td>
<td>7.4 ± 5.3</td>
</tr>
<tr>
<td>Baseline Stenosis ± SD</td>
<td>72.7% ± 18.1</td>
<td>75.9% ± 20.0</td>
<td>0.015</td>
<td>73.6% ± 18.7</td>
</tr>
<tr>
<td>Calcification</td>
<td>37.1%</td>
<td>37.1%</td>
<td>1.000</td>
<td>37.1%</td>
</tr>
</tbody>
</table>

### Definitive LE Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Flow-limiting Dissections</th>
<th>Bail-out stenting</th>
<th>Primary Patency** at 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Claudicants</td>
<td>2.2%</td>
<td>3.2% (33/1022)</td>
<td>78%</td>
</tr>
<tr>
<td>All CLI Patients</td>
<td>2.5%</td>
<td></td>
<td>71%</td>
</tr>
</tbody>
</table>

*Primary patency by duplex ultrasound at 12 months (PSVR ≤2.4 with no clinically-driven reintervention)

** Patency value determined by Kaplan-Meier analysis

**Definitive AR – Study design**

### General and Angiographic Criteria Assessment

- **Lesion severely calcified?**
  - **NO**
  - **YES**

### Randomization

- **DA+DCB** (n=48)
- **DCB** (n=54)
- **DA+DCB** (n=19)

*Defined as: dense circumferential calcification extending > 5 cm

### Inclusion Criteria
- RCC Score of 2, 3 or 4
- \( \geq 70\% \) stenosis, restenosis or occlusion in the SFA and/or popliteal artery
- Target lesion(s) length is 7-15 cm
- Target vessel diameter is \( \geq 4 \text{ mm} \) and \( \leq 7 \text{ mm} \)

### Exclusion Criteria
- In-stent restenosis
- Aneurysmal target vessel
- 2 or more lesions that require treatment in the target limb

---

Zeller, T. Definitive AR 12 mo Results. VIVA Nov. 2014 SC1770102014A.
## Definitive AR – Baseline and Outcomes

<table>
<thead>
<tr>
<th>Baseline Demographics</th>
<th>DA+DCB (N=48)</th>
<th>DCB (N=54)</th>
<th>p-Value*</th>
<th>DA+DCB Severe Ca++ (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length (cm)</td>
<td>11.2</td>
<td>9.7</td>
<td>0.05</td>
<td>11.9</td>
</tr>
<tr>
<td>Calcification</td>
<td>70.8%</td>
<td>74.1%</td>
<td>0.82</td>
<td>94.7%</td>
</tr>
<tr>
<td>Severe calcification</td>
<td>25.0%</td>
<td>18.5%</td>
<td>0.48</td>
<td>89.5%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>DA+DCB (N=48)</th>
<th>DCB (N=54)</th>
<th>p-Value*</th>
<th>DA+DCB Severe Ca++ (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical Success</td>
<td>89.6%</td>
<td>64.2%</td>
<td>0.004</td>
<td>84.2%</td>
</tr>
<tr>
<td>Bail-Out Stent</td>
<td>0% (0/48)</td>
<td>3.7% (2/54)</td>
<td>0.50</td>
<td>5.3% (1/19)</td>
</tr>
<tr>
<td>Dissection (flow limiting, Grade C/D)</td>
<td>2% (1/48)</td>
<td>19% (10/54)</td>
<td>0.01</td>
<td>0% (0/19)</td>
</tr>
</tbody>
</table>

* p-value for DA+DCB RCT and DCB groups

Technical success defined as achieving ≤30% residual stenosis following protocol-defined treatment and before adjunctive therapy (ie post-dilatation). No surgical interventions were required for any patient.

Zeller, T. Definitive AR 12 mo Results. VIVA Nov. 2014 SC1770102014A.
Definitive AR – 12 Month Outcomes
Angiographic Patency

Results for all patients who returned for angiographic follow-up

Per Core Lab Assessment. “All Severe Ca++ “ group includes all patients treated with DA+DCB therapy including randomized and non-randomized patients with severe calcium.

Zeller, T. Definitive AR 12 mo Results. VIVA Nov. 2014 SC1770102014A.
Definitive AR – 12 Month Outcomes

Increased lumen gain with Directional Atherectomy before DCB resulted in improved patency at 12 months*

* Includes all patients that received DA+DCB in both randomized and non-randomized arms

G. Tepe LINC 2017
Summary

- Latest 5 year results from IN.PACT SFA trial and 3 year results from the IN.PACT Global study show a sustained clinical benefit of IN.PACT Admiral

- Current data suggest an added benefit of Vessel preparation, especially when treating long, challenging lesions

- Evidence points to the benefits of using directional Atherectomy followed by DCB to prepare vessel for drug uptake and minimize dissection rate and need for provisional stenting
Clinical evidence of IN.PACT and opportunities of DAART for the treatment of PAD

Michel Bosiers MD
Vascular and endovascular surgeon
St- Franziskus-Hospital Münster, Germany
Director: Prof. G. Torsello
Clinical evidence of IN.PACT and opportunities of DAART for the treatment of PAD

Michel Bosiers MD
Vascular and endovascular surgeon
St- Franziskus-Hospital Münster, Germany
Director: Prof. G. Torsello