Leave Nothing Behind 2.0: Combination Therapy To Advance SFA Treatment Strategy

SFA disease management: Are the Long term outcomes with IN.PACT DCB Changing the Peripheral Landscape

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Bad Krozingen, Germany
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- **Honoraria received from:** Abbott Vascular, Bard Peripheral Vascular, Veryan, Biotronik, Boston Scientific Corp., Cook Medical, Gore & Associates, Medtronic, Spectranetics, TriReme, VIVA Physicians, GLG, Philips, Shockwave, Intact

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Background

• Drug-coated balloons (DCBs) have significantly changed the management of symptomatic peripheral arterial disease

• DCBs have shown improved outcomes over angioplasty at 1 and 2 years\(^1\)-\(^7\) in RCTs, with the IN.PACT Admiral DCB showing sustained and durable treatment benefit through 4 years\(^8\),\(^9\)

• Beyond RCTs, real world registries enrolling more complex disease, show an increased reliance to provisional stenting\(^10\)-\(^12\)

1. Tepe G. et al., Circulation. 2015.
2. Laird et al., J Am Coll Cardiol. 2015.
4. Laurich C. LEVENT II 2 Year Results, SVS 2015.
7. Brodmann M, ILLUMENATE EU RCT 2 Year Results VIVA 2017
8. Schneider P et al., 2018;11:e005891 Circulation CI
9. Schneider, P. IN.PACT SFA 4 Year Results, VIVA 2017
10. Scheinert D. IN.PACT Global LL, EuroPCR 2015
11. Tepe G. IN.PACT Global CTO, CX 2016
### Worldwide Available DCBs

**Selected Products**

DCBs have demonstrated promising results at 1- and 2-years in randomized trials. Longer-term data for commercially available DCBs are limited.

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>DCB</th>
<th>Dose (μg/mm²)</th>
<th>Excipient</th>
<th>RCT Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BARD</strong></td>
<td>Lutonix</td>
<td>2.0</td>
<td>Polysorbate/Sorbitol</td>
<td>1- and 2-year</td>
</tr>
<tr>
<td><strong>Medtronic</strong></td>
<td>IN.PACT</td>
<td>3.5</td>
<td>Urea</td>
<td>1-, 2-, 3-, 4-year</td>
</tr>
<tr>
<td><strong>Spectranetics</strong></td>
<td>Stellarex</td>
<td>2.0</td>
<td>Polyethylene Glycol</td>
<td>1- and 2-year</td>
</tr>
<tr>
<td><strong>Boston Scientific</strong></td>
<td>Ranger</td>
<td>2.0</td>
<td>Citrate Ester</td>
<td></td>
</tr>
<tr>
<td><strong>BIOTRONIK</strong></td>
<td>Passeo-18 Lux</td>
<td>3.0</td>
<td>BTHC</td>
<td></td>
</tr>
<tr>
<td><strong>B Braun</strong></td>
<td>SeQuent Please OTW</td>
<td>3.0</td>
<td>Resveratrol</td>
<td></td>
</tr>
<tr>
<td><strong>iVascular</strong></td>
<td>Luminor</td>
<td>3.0</td>
<td>Ester</td>
<td></td>
</tr>
<tr>
<td><strong>COOK</strong></td>
<td>Advance 18 PTX</td>
<td>3.0</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td><strong>Aachen Resonance</strong></td>
<td>Elutax SV</td>
<td>2.2</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td><strong>BIOSENSORS</strong></td>
<td>BioPath (FREEWAY)</td>
<td>3.0</td>
<td>Shellac</td>
<td></td>
</tr>
<tr>
<td><strong>CARDIONOVUM</strong></td>
<td>Legflow</td>
<td>3.0</td>
<td>Shellac</td>
<td></td>
</tr>
</tbody>
</table>

1. Tepe G. et al., Circulation. 2015.
2. Laird et al., J Am Coll Cardiol. 2015.
4. Laurich C. LEVENT II 2 Year Results, SVS 2015.
8. Schneider, P. IN.PACT SFA 4 Year Results, VIVA 2017.
**FDA Approved Drug-Coated Balloons**

**Summary of Multicenter RCTs**

- **LEVANT II**: PSVR ≤ 2.5 and freedom from TLR\(^1\)-\(^2\)
- **IN.PACT SFA**: PSVR ≤ 2.4 and freedom from CD-TLR\(^3\)-\(^5\)
- **ILLUMENATE EU and US RCTs**: PSVR ≤ 2.5 and freedom from CD-TLR\(^6\)-\(^7\)

<table>
<thead>
<tr>
<th></th>
<th>LEVANT II Trial(^1)-(^2)</th>
<th>IN.PACT SFA Trial(^3)-(^5)</th>
<th>ILLUMENATE EU RCT(^6)</th>
<th>ILLUMENATE Pivotal(^7)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1-yr</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lutonix O35</td>
<td>73.5%</td>
<td>IN.PACT Admiral</td>
<td>87.5%</td>
<td>Stellarex</td>
</tr>
<tr>
<td></td>
<td>△16.7% P&lt;0.001</td>
<td>△31.7% P&lt;0.001</td>
<td>△24.0% P&lt;0.001</td>
<td>△11.4% P&lt;0.002</td>
</tr>
<tr>
<td>PTA</td>
<td>56.8%</td>
<td>55.8%</td>
<td>65.0%</td>
<td>70.9%</td>
</tr>
<tr>
<td><strong>2-yr</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lutonix O35</td>
<td>58.6%</td>
<td>IN.PACT Admiral</td>
<td>78.9%</td>
<td>Stellarex</td>
</tr>
<tr>
<td></td>
<td>△5.6% P&lt;0.05</td>
<td>△28.8% P&lt;0.001</td>
<td>△14.0% P&lt;0.004</td>
<td>△11.4% P&lt;0.002</td>
</tr>
<tr>
<td>PTA</td>
<td>53.0%</td>
<td>50.1%</td>
<td>61.2%</td>
<td></td>
</tr>
<tr>
<td><strong>3-yr</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IN.PACT Admiral</td>
<td>69.5%</td>
<td>△24.4% P&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTA</td>
<td>45.1%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Primary patency rates derived from respective trials’ Kaplan Meier estimates.

IN.PACT SFA Trial: Overview

Objective: Assess the safety and efficacy of IN.PACT™ Admiral™ DCB vs. standard PTA for the treatment of superficial femoral and proximal popliteal artery disease due to claudication and rest pain

- Prospective, multicenter EU and US, randomized (2:1), single-blinded trial
- 331 patients enrolled:
  - IN.PACT™ Admiral™ DCB (n = 220) vs. PTA (n = 111)
- Rutherford Clinical Category 2-4
- Lesion lengths 4-18 cm or occlusions ≤ 10 cm
- Subjects followed up to 5 years
- Independent and blinded core labs and clinical events committee:
  - Duplex Ultrasound Core Lab: VasCore DUS Core Laboratory; Boston, MA, USA
  - Angiographic Core Lab: SynvaCor Angiographic Core Laboratory; Springfield, IL, USA
  - Clinical Events Committee and Data Safety Monitoring: HCRI; Boston, MA, USA

IN.PACT SFA Trial
Primary Patency\(^1\) Results Through 3 Years

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 the 30-day window prior to each follow-up interval

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Schneider P et al. 2018;11:e005891 Circulation CI
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
## IN.PACT SFA Trial
### Additional Outcomes Through 4 Years

<table>
<thead>
<tr>
<th></th>
<th>IN.PACT DCB (N=220)</th>
<th>PTA (N=111)</th>
<th>P-value(^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically-driven TLR (^1)</td>
<td>23.4% (43/184)</td>
<td>31.1% (32/103)</td>
<td>0.164</td>
</tr>
<tr>
<td>Any TLR (^2)</td>
<td>24.5% (45/184)</td>
<td>34.0% (35/103)</td>
<td>0.100</td>
</tr>
<tr>
<td>Time to First CD-TLR</td>
<td>739.2 ± 384.0</td>
<td>302.9 ± 213.0</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### Time to First CD-TLR

- **IN.PACT DCB**: 739.2 days
- **PTA**: 302.9 days

**DOUBLE Time to first reintervention with IN.PACT DCB**

\(^1\) P-value
\(^2\) Any TLR
Robust IN.PACT™ Admiral™ DCB Clinical Program

IN.PACT DCB Clinical Data for the SFA

RCTs + Approval Studies

IN.PACT SFA 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

Real-World Study
IN.PACT Global Study Overview

Real-world, prospective, multicenter, single arm study with independent adjudication to expand clinical evidence of the IN.PACT™ Admiral™ DCB in the treatment of patients with femoropopliteal lesions.

- Independent adjudication by Clinical Events Committee
- Prospective subset analysis with core lab reported results (de novo ISR, long lesions ≥15 cm, CTOs ≥5 cm)

All-comers RCC 2-4
- Bilateral disease
- Multiple lesions
- SFA and Popliteal
- TASC A, B, C, D
- De novo ISR
- Long Lesions
- CTOs

1535 Subjects Enrolled
- 150 mm DCB Cohort 119 Subjects
- 1416 Subjects
- VIVA 2016 M. Jaff
- De novo ISR 131 Subjects
- Long Lesion (≥15 cm) 157 Subjects
- CTO (≥5 cm) 126 Subjects
- VIVA 2015 M. Brodmann
- EuroPCR 2015 D. Scheinert
- Charing Cross 2016 G. Tepe

*Analysis is based on the 1406 ITT subjects.
1Syntactx Clinical Events Committee, New York, NY, US; 2VasCore DUS Core Lab, Boston, MA, US; 3SynvaCor Angiographic Core Lab, Springfield, IL, US
Jaff, M. VIVA 2016
IN.PACT Global Study

Freedom from CD-TLR $^1$ Through 2 Years

1. Number at risk represents the number of evaluable subjects at the beginning of the each 60-day window
### IN.PACT Clinical Program

#### 12-month Outcomes

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Study Description</th>
<th>12-Month Patency</th>
<th>12-Month CD-TLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCTs</td>
<td>IN.PACT SFA (EU+US)</td>
<td>87.5%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Approval Study</td>
<td>IN.PACT Japan</td>
<td>93.9%</td>
<td>2.9%</td>
</tr>
<tr>
<td></td>
<td>IN.PACT China</td>
<td>90.2%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Pre-Specified Cohorts</td>
<td>Long Lesion</td>
<td>91.1%</td>
<td>6.0%</td>
</tr>
<tr>
<td></td>
<td>ISR</td>
<td>88.7%</td>
<td>7.3%</td>
</tr>
<tr>
<td></td>
<td>CTO</td>
<td>85.3%</td>
<td>11.3%</td>
</tr>
<tr>
<td></td>
<td>Belgian</td>
<td>NR</td>
<td>7.6%</td>
</tr>
<tr>
<td></td>
<td>ASEAN</td>
<td>NR</td>
<td>3.8%</td>
</tr>
</tbody>
</table>

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2. Iida O et al. JEVT, 2017:1526602817745565
3. Presented by Chen Z. VEITH 2017
**DCB “Real-World” Registries**

Global registries include real-world patients and lesions

<table>
<thead>
<tr>
<th>Key Inclusion Criteria</th>
<th>Global¹</th>
<th>Long Lesion²</th>
<th>Long Lesion³</th>
<th>CTO⁴</th>
<th>ISR⁵</th>
<th>Clinical⁶</th>
<th>ILLUMENATE Global⁷</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCC ≤4 SFA &amp; PA</td>
<td>RCC 2-4 SFA &amp; PA</td>
<td>RCC 2-4 SFA &amp; PA</td>
<td>RCC 2-4 SFA &amp; PA CTOs</td>
<td>RCC 2-4 SFA &amp; PA ISR</td>
<td>RCC 2-4 SFA &amp; PA</td>
<td>RCC 2-4 SFA &amp; PA</td>
<td></td>
</tr>
<tr>
<td>Key Patient Characteristics</td>
<td>68.3y</td>
<td>67.6y</td>
<td>69.5y</td>
<td>67.5y</td>
<td>67.8y</td>
<td>68.6y</td>
<td>68.2y</td>
</tr>
<tr>
<td>Age (years)</td>
<td>9.0%</td>
<td>6.1%</td>
<td>16.7%</td>
<td>11.1%</td>
<td>10.0%</td>
<td>11.0%</td>
<td>8.6%</td>
</tr>
<tr>
<td>RCC ≥4 (%)</td>
<td>67.6%</td>
<td>73.7%</td>
<td>66.2%</td>
<td>69.0%</td>
<td>69.5%</td>
<td>67.8%</td>
<td>73.0%</td>
</tr>
<tr>
<td>Men (%)</td>
<td>39.5%</td>
<td>36.4%</td>
<td>41.0%</td>
<td>29.6%</td>
<td>35.1%</td>
<td>39.9%</td>
<td>33.7%</td>
</tr>
<tr>
<td>DM (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Key Lesion Characteristics</td>
<td>10.1cm</td>
<td>21.3cm</td>
<td>26.4cm</td>
<td>22.9cm</td>
<td>17.2cm</td>
<td>12.1cm</td>
<td>7.5cm</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>31.2%</td>
<td>52.1%</td>
<td>60.4%</td>
<td>100.0%</td>
<td>34.0%</td>
<td>35.5%</td>
<td>31.3%</td>
</tr>
<tr>
<td>CTO (%)</td>
<td>50.2%</td>
<td>78.9%²</td>
<td>71.8%</td>
<td>71.0%</td>
<td>59.1%</td>
<td>68.7%</td>
<td>56.2%³</td>
</tr>
<tr>
<td>Ca²⁺ (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

2. Bard Lutonix Instructions for Use BAW1387400r3, Section 10.5. Moderate to severe calcification reported; amputations not reported (NR).
**DCB “Real-World” Registries**

Similar outcomes despite potential differences in populations and lesions, as well as reliance on provisional stenting

<table>
<thead>
<tr>
<th>12-mo Outcomes</th>
<th>Global&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Long Lesion&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Long Lesion&lt;sup&gt;3&lt;/sup&gt;</th>
<th>CTO&lt;sup&gt;4&lt;/sup&gt;</th>
<th>ISR&lt;sup&gt;5&lt;/sup&gt;</th>
<th>Clinical&lt;sup&gt;6&lt;/sup&gt;</th>
<th>ILLUMINATE Global&lt;sup&gt;7&lt;/sup&gt; Stellarex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up</td>
<td>Complete follow-up</td>
<td>107 &amp; 102 subjects for safety &amp; effectiveness, respectively; Core lab-adjudicated</td>
<td>157 subjects Complete follow-up; Core lab-adjudicated</td>
<td>126 subjects Complete follow-up; Core lab-adjudicated</td>
<td>131 subjects Complete follow-up; Core lab-adjudicated</td>
<td>1406 subjects Complete follow-up; CEC &amp; site-reported outcomes</td>
<td>371 subjects Complete follow-up; Core lab-adjudicated</td>
</tr>
<tr>
<td>1&lt;sup&gt;st&lt;/sup&gt; Patency (%)</td>
<td>691 subjects</td>
<td>68.9%</td>
<td>91.1%</td>
<td>85.3%</td>
<td>88.7%</td>
<td>NR</td>
<td>81.4%</td>
</tr>
<tr>
<td>FF TLR/CD-TLR (%)</td>
<td>94.3%</td>
<td>87.8%</td>
<td>94.0%</td>
<td>89.1%</td>
<td>92.9%</td>
<td>92.6%</td>
<td>94.8%</td>
</tr>
<tr>
<td>Bail-out Stent (%)</td>
<td>25.2%</td>
<td>39.8%</td>
<td>40.4%</td>
<td>46.8%</td>
<td>14.5%</td>
<td>25.3%</td>
<td>17.3%</td>
</tr>
<tr>
<td>Amputations (%)</td>
<td>0.5% (3/632)</td>
<td>NR</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.2% (3/1311)</td>
<td>0.3% (1/371)</td>
</tr>
</tbody>
</table>

2. Bard Lutonix Instructions for Use BAW1387400r3, Section 10.5. Moderate to severe calcification reported; amputations not reported (NR).
DCB “Real-World” Registries

Similar outcomes despite potential differences in populations and lesions, as well as reliance on provisional stenting
Consistently low frequency of major amputation across platforms

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Global¹</th>
<th>Long Lesion²</th>
<th>Long Lesion³</th>
<th>CTO⁴</th>
<th>ISR⁵</th>
<th>Clinical⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>691 subjects</td>
<td>107 &amp; 102 subjects</td>
<td>157 subjects</td>
<td>126 subjects</td>
<td>131 subjects</td>
<td>1406 subjects</td>
</tr>
<tr>
<td></td>
<td>Complete follow-up</td>
<td>Complete follow-up; Core lab-adjudicated</td>
<td>Complete follow-up; Core lab-adjudicated</td>
<td>Complete follow-up; Core lab-adjudicated</td>
<td>Complete follow-up; CEC &amp; site-reported outcomes</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>12-mo Outcomes</th>
<th>Global¹</th>
<th>Long Lesion²</th>
<th>Long Lesion³</th>
<th>CTO⁴</th>
<th>ISR⁵</th>
<th>Clinical⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° Patency (%)</td>
<td>NR</td>
<td>68.9%</td>
<td>91.1%</td>
<td>85.3%</td>
<td>88.7%</td>
<td>NR</td>
</tr>
<tr>
<td>FF TLR/CD-TLR(%)</td>
<td>94.3%</td>
<td>87.8%</td>
<td>94.0%</td>
<td>89.1%</td>
<td>92.9%</td>
<td>92.6%</td>
</tr>
<tr>
<td>Bail-out Stent (%)</td>
<td>25.2%</td>
<td>39.8%</td>
<td>40.4%</td>
<td>46.8%</td>
<td>14.5%</td>
<td>25.3%</td>
</tr>
<tr>
<td>Amputations (%)</td>
<td>0.5% (3/632)</td>
<td>NR</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.2% (3/1311)</td>
</tr>
</tbody>
</table>

2. Bard Lutonix Instructions for Use BAW1387400r3, Section 10.5. Moderate to severe calcification reported; amputations not reported (NR).
Treatment Algorithm in TASC C & D Femoro-Popliteal Lesions

Vessel Preparation (lesion specific)
(PTA, Specialty Balloon, Directional Atherectomy)

In case of severe dissection / recoil

Good result

DES / Supera / Viabahn

DCB according to the RVD + 1mm

Atherectomy & DCB

Additional BMS on indication
Conclusion

• DCBs have become the mainstay in my treatment algorithm for the SFA
• Allowing for aggressive treatment of more complex disease
• Decreased the use of stents
• DCBs afford interventionalist the ability to practice “leave nothing behind” preserving future treatment options
Leave Nothing Behind 2.0: Combination Therapy To Advance SFA Treatment Strategy

SFA disease management: Are the Long term outcomes with IN.PACT DCB Changing the Peripheral Landscape

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