The Reality of PAD: Treatment Strategies for Improved Outcomes

January 26, 2021
15:05 pm – 16:35 pm CET

Moderator: Dierk Scheinert, MD
Leipzig, Germany

Operator: Andrej Schmidt, MD
Leipzig, Germany

Panel:
Ralf Langhoff, MD
Berlin, Germany
Ravish Sachar MD
Raleigh, NC
Giovanni Torsello, MD
Münster, Germany
Thomas Zeller MD
Bad Krozingen, Germany
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### Agenda

**The Reality of PAD: Treatment Strategies for Improved Outcomes**

**Panel:** Thomas Zeller, MD, Giovanni Torsello, MD, Ralf Langhoff, MD, Ravish Sachar, MD

| Introduction | Dierk Scheinert, MD  
Universitätsklinikum Leipzig, Leipzig, Germany |
|--------------|---------------------------------------------------|
| Live Case: Use of Directional Atherectomy and IN.PACT™ Admiral™ DCB for Long, Calcified Lesion | Andrej Schmidt, MD  
Universitätsklinikum Leipzig, Leipzig, Germany |
| Redefining the Management of PAD: A Critical Look at Calcium | Ralf Langhoff, MD  
Sankt Gertrauden Krankenhaus, Berlin, Germany |
| Clinical Evidence for Vessel Preparation Followed by DCB in the Most Challenging Lesions | Ravish Sachar, MD  
North Carolina Heart & Vascular, UNC-Rex Healthcare, Raleigh, NC |
| What is the Clinical Evidence for Long-term Effectiveness of DCB to Reduce Reinterventions? | Giovanni Torsello, MD  
St. Franziskus-Hospital, Münster, Germany |
| Additional Strategies, Tools & Techniques for Peripheral Vascular Therapies: A Pre-Recorded Case | Thomas Zeller, MD  
Universitäts Herzzentrum Freiburg-Bad Krozingen, Bad Krozingen, Germany |
| Discussion | Panel |
| Closing | Dierk Scheinert, MD |

**Case Operator** - Andrej Schmidt, MD

**Moderator** - Dierk Scheinert, MD
Redefining the Management of PAD: A Critical Look at Calcium

Ralf Langhoff, MD
Sankt Gertrauden Hospital
Berlin, Germany
Challenges Associated with Severe Calcium in Practice

**Procedural Obstacles**
- Endovascular strategies are challenged in the presence of calcification
- High lesion complexity
- Difficult lesion crossing
- Highly resistive plaque
- Extended intervention time

**Outcome Limitations**
- Dissection
- Provisional stenting
- Stent fractures
- Residual stenosis / re-stenosis
- Drug-coated balloon effectiveness (decreased absorption)

2. Scheinert D et al. CIRC CI 2018;11:1-10
Limitations of Calcium for Endovascular Therapy

- Calcium is a potential barrier to optimal drug absorption
- Calcium distribution and severity may affect late lumen loss (LLL) and primary patency

Primary patency defined as freedom from restenosis by duplex based on PSVR<2.4 and TLR


- Primary patency defined as freedom from restenosis by duplex based on PSVR<2.4 and TLR
How is Calcification Addressed in DCB Clinical Trials?
## Clinical Trial Angiography Core Labs

<table>
<thead>
<tr>
<th>Beth Israel</th>
<th>SynvaCor</th>
<th>Genae Associates, Belgium</th>
<th>No Core Lab</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILLUMENATE US</td>
<td>LEVANT 2</td>
<td>LEVANT 1 (FIH)</td>
<td>LEVANT Global</td>
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<td>ILLUMENATE Global</td>
<td>IN.PACT SFA</td>
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<td>Ranger Global</td>
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<td>IN.PACT Global Imaging Cohorts</td>
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<td>ILLUMENATE EU</td>
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<td>ILLUMENATE FIH</td>
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Core Lab Definitions of Severe Calcium Vary

<table>
<thead>
<tr>
<th>Beth Israel¹⁻³</th>
<th>SynvaCor⁴⁻¹¹</th>
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<tbody>
<tr>
<td><strong>Severe calcification:</strong></td>
<td><strong>Severe calcification:</strong></td>
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<tr>
<td>▪ Radiopacities noted on both sides of the arterial wall and extending more than 1 cm of length prior to contrast injection or digital subtraction.</td>
<td>▪ Calcium visible along both sides of the arterial wall</td>
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<td>▪ Covers 2 cm or greater of the target lesion area</td>
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<td>▪ Encompasses greater than 50% of the total target lesion treatment area by visual estimate and/or the calcium is circumferential (360°) in nature</td>
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<td>▪ on both sides of the vessel lumen extending 2 cm or greater on a single AP view OR</td>
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<td></td>
<td>▪ Classified as exophytic calcification, significantly impedes blood flow in the vessel.</td>
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10. Scheinert, D. et al. CIRC-Cardiovasc Interv 2018;11  
## Calcium Grading System

**Bilateral Calcification**

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<thead>
<tr>
<th>Severe calcification:</th>
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<th>Severe calcification:</th>
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<td></td>
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<tr>
<td></td>
<td>Classified as exophytic calcification, significantly impedes blood flow in the vessel.</td>
<td>Classified as exophytic calcification, significantly impedes blood flow in the vessel.</td>
</tr>
</tbody>
</table>

### Grading System: Severe Calcification

**Grade 3:** bilateral calcification < 5 cm; a) intimal calcification; b) medical calcification; c) mixed type

**Grade 4:** bilateral calcification ≥ 5 cm; a) intimal calcification; b) medical calcification; c) mixed type

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10. Scheinert, D. et al. CIRC-Cardiovasc Interv 2018;11
Summary

- Presence of calcium in the peripheral vasculature poses a significant challenge to current endovascular device strategies.
- Results from contemporary DCB studies show promising outcomes when treating calcified lesions, however comparisons of calcium across these trails are futile given differences in calcium definitions and differences in adjudication.
- Need for consensus on how calcium is defined.

Is calcium the Achilles heel of endovascular treatment strategies or is there an option? Current strategies to remove calcium before application of antiproliferative therapy.
Thank You
Clinical Evidence for Vessel Preparation Followed by DCB in the Most Challenging Lesions

Ravish Sachar, MD
North Carolina Heart & Vascular,
UNC-Rex Healthcare
Raleigh, NC
Meeting the Challenge of Complex Lesion Morphologies

Complex Lesions are Often Long and Heavily Calcified

Severe Calcification

Long Lesions/CTOs

Directional Atherectomy + Anti-Restenotic Therapy
DEFINITIVE AR Pilot Study

**121 Participants (RCC 2-4)**

- **Lesions Severely Calcified?**
  - No
  - Yes

**Randomized arm**
- 102 Participants
  - DA + DCB: 48 Participants
  - DCB: 54 Participants
  - NR DA + DCB: 19 Participants

**Non-randomized (NR) arm**
- 19 Participants

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**12-Month Angiographic Patency**

- **All Subjects**
  - DA + DCB: 82.4%
  - DCB: 71.8%
  - Total: 68.8%

- **Lesion >10 cm**
  - DA + DCB: 95.0%
  - DCB: 68.8%

- **All Severe Ca++ Lesions**
  - DA + DCB: 58.3%
  - DCB: 42.9%

- **Non-Randomized Severe Ca++ Lesions**
  - DA + DCB: 50.0%

DA, Directional Atherectomy; DCB, Drug-Coated Balloons; NR, Non-randomized.
REALITY Study

Objective
Evaluate the effectiveness of the HawkOne™ directional atherectomy system followed by the IN.PACT™ Admiral™ drug-coated balloon to debulk moderate and severely calcified femoropopliteal artery atherosclerotic lesions.

Primary Endpoints
Effectiveness:
Primary Patency at 12 months²
Safety:
Freedom from Major Adverse Events (MAE) through 30 days³

Study Design
- 102 Subjects, 13 sites across the US & Germany
- Prospective, non-randomized, single-arm angiographic and duplex ultrasound core lab adjudicated
- Change in maximal luminal plaque area adjudicated by an independent intravascular ultrasound core lab

1. Sponsored and conducted by VIVA Physicians; funded by Medtronic.
2. Primary patency defined as freedom from restenosis (DUS peak systolic velocity ratio >2.4) and CD-TLR, defined as any reintervention to the target lesion due to a return of symptoms and/or ankle-brachial index (ABI) decrease of 20% or > 0.15 when compared with the post index procedure baseline ABI.
3. Major Adverse Events (MAE) defined as flow-limiting dissections (D-F), vessel perforation(s) requiring bare metal stents or stent-grafts implantation, unplanned major amputation, intra-procedure distal atheroembolization and CD-TVR.
REALITY Study Data¹
Baseline Lesion and Clinical Characteristics

Key Characteristics

Peripheral Arterial Calcification Scoring System (PACSS)²

- Bilateral Calcium [PACSS 3 & 4]
  - 86.2%
- Bilateral Calcium ≥5cm [PACSS 4]
  - 67.6%

Lesion Length
- 17.9cm

Occlusions
- 39.0%

Baseline Diameter Stenosis
- 88.8%

Age
- 69.6 yrs

Hypertension
- 89.2%

Hyperlipidemia
- 81.4%

Renal Disease
- 15.7%

Diabetes Mellitus
- 53.9%

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¹ Rocha-Singh, K. LINC 2020
² Rocha-Singh, K. et al., Catheter Cardiovasc Interv. 2014 May 1;83(6):e212-20
REALITY Study – Unmatched Calcium and Long Lesions

With a focus on long and complex lesions, the REALITY study was designed to explore the boundaries of endovascular therapy.

1. Sponsored and conducted by VIVA Physicians; funded by Medtronic. REALITY data presented by Rocha-Singh, K. LINC 2020
2. Calcium definitions differ across studies. These are angiographic, core lab adjudicated reported calcium results. This graph is for illustration purposes only. References are at the end of this presentation.
The REALITY Study examines the challenge of treating long, heavily calcified lesions with HawkOne directional atherectomy system and IN.PACT Admiral drug-coated balloon.

<table>
<thead>
<tr>
<th>Procedural Characteristics</th>
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<tbody>
<tr>
<td>Perforations</td>
<td>3.1% (3/98)</td>
</tr>
<tr>
<td>Dissection ≥ Grade C</td>
<td>14.3% (14/98)</td>
</tr>
<tr>
<td>Distal Embolization</td>
<td>12.8% (11/86)</td>
</tr>
<tr>
<td><strong>Provisional Stenting</strong></td>
<td><strong>8.8% (9/102)</strong></td>
</tr>
</tbody>
</table>
**REALITY Study**

Primary Effectiveness Outcomes

1. Sponsored and conducted by VIVA Physicians; funded by Medtronic.
2. Primary patency defined as freedom from restenosis (DUS peak systolic velocity ratio >2.4) and CD-TLR, defined as any reintervention to the target lesion due to a return of symptoms and/or ankle-brachial index (ABI) decrease of 20% or > 0.15 when compared with the post index procedure baseline ABI.
3. 12-month data include patients beyond the follow-up window. Red lines indicate the 12-month follow-up window.
REALITY Study – Unmatched Calcium and Long Lesions

1. Calcium definitions differ across studies. These are angiographic, core lab adjudicated reported calcium results. This graph is for illustration purposes only. References are at the end of this presentation.

UNMATCHED LESIONS
86.2% 17.9cm 39.0%
Bilateral Calcium Average Lesion Length Chronic Total Occlusion

COMPELLING OUTCOMES
92.6% 76.7%
FF-CD TLR Patency
12-month data include patients beyond the follow-up window.

PRESERVED TREATMENT OPTIONS
8.8%
Bailout Stent Rate

Summary

- The REALITY Study investigated the use of directional atherectomy using the HawkOne device followed by IN.PACT Admiral DCB in unmatched long and calcified lesions.

- The REALITY Study demonstrated that this vessel preparation treatment strategy is effective up to 12-months with an acceptable safety profile.

- The directional atherectomy vessel preparation strategy used in the REALITY Study is associated with a low provisional stent rate.
Thank You
What is the Clinical Evidence for Long-term Effectiveness of DCB to Reduce Reinterventions?

Giovanni Torsello, MD
St. Franziskus-Hospital
Münster, Germany
### Long-term Patency and CD-TLR Outcomes in DCB IDE Studies

#### IN.PACT Admiral DCB: Long-Term Data

<table>
<thead>
<tr>
<th>Device Type</th>
<th>1-Year</th>
<th>2-Year</th>
<th>3-Year</th>
<th>4-Year</th>
<th>5-Year</th>
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<tbody>
<tr>
<td><strong>Primary Patency</strong> (K-M Estimates)</td>
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<tr>
<td>IN.PACT IDE</td>
<td>87.5%¹</td>
<td>79.0%¹</td>
<td>69.5%¹</td>
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<tr>
<td>IN.PACT DCB</td>
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<tr>
<td>LEVANT IDE</td>
<td>73.5%²</td>
<td>58.6%³</td>
<td>not reported</td>
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<tr>
<td>Lutonix DCB</td>
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<tr>
<td>ILLUMENATE IDE</td>
<td>82.3%⁴</td>
<td>72.1%⁵</td>
<td>64.2%⁶</td>
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<tr>
<td>Stellarex DCB</td>
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<td>RANGER II IDE</td>
<td>89.8%⁷</td>
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<tr>
<td>Ranger DCB</td>
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<tr>
<td>CD-TLR</td>
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<tr>
<td>IN.PACT IDE</td>
<td>2.4%¹</td>
<td>9.1%¹</td>
<td>15.2%¹</td>
<td>23.4%¹</td>
<td>25.5%¹</td>
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<tr>
<td>IN.PACT DCB</td>
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<tr>
<td>LEVANT IDE</td>
<td>12.3%²</td>
<td>18.0%³</td>
<td>not reported</td>
<td>not reported</td>
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<td>Lutonix DCB</td>
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<tr>
<td>ILLUMENATE IDE</td>
<td>7.9%⁴</td>
<td>not reported</td>
<td>not reported</td>
<td>28.2%⁸</td>
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<tr>
<td>Stellarex DCB</td>
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<tr>
<td>RANGER IDE</td>
<td>5.5%⁷</td>
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<tr>
<td>Ranger DCB</td>
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</table>

3. Laurich C. LEVANT 2 Two-Year Results; SVS 2015.*Reported as a freedom-from rate
5. Mathews SJ. ILLUMENATE Pivotal Two-Year Results Presentation; NCVH 2018.
8. Lyden S. ILLUMENATE Pivotal 4-year Results Presentation; LINC 2020.

Results are not directly comparable, for illustration purposes only.
IN.PACT Global Study Full Clinical Cohort
Freedom from Reintervention

Sustained Effectiveness Through 5 Years

This presentation includes outcome data on the 1406 ITT subjects who comprise the IN.PACT Global Clinical Cohort.

# IN.PACT Global Study Full Clinical Cohort

## Safety Through 5 Years

### IN.PACT Global

**N= 1406 Subjects**

<table>
<thead>
<tr>
<th>Event</th>
<th>K-M Cumulative Incidence*</th>
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</thead>
<tbody>
<tr>
<td>Primary Safety Composite¹</td>
<td>67.4% (392)</td>
</tr>
<tr>
<td>CD-TLR² %</td>
<td>30.6 (366)</td>
</tr>
<tr>
<td>Any TLR³ %</td>
<td>31.3 (374)</td>
</tr>
</tbody>
</table>

* Percent based on K-M estimate (number of subjects with event).
1. Safety composite endpoint consists of: Freedom from device- and procedure-related death to 30 days, freedom from major target limb amputation within 80 months; and freedom from CD-TVR within 80 months.
2. Clinically-driven TLR adjudicated by an independent Clinical Event Committee and defined as any re-intervention within 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.

### IN.PACT Global

**N= 1406 Subjects**

<table>
<thead>
<tr>
<th>Event</th>
<th>K-M Cumulative Incidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Adverse Events¹</td>
<td>45.9% (589)</td>
</tr>
<tr>
<td>CEC Adjudicated All-cause Death</td>
<td>19.5% (244)</td>
</tr>
<tr>
<td>CD-TVR</td>
<td>31.9% (381)</td>
</tr>
<tr>
<td>Major Target Limb Amputation</td>
<td>1.7% (19)</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>5.7% (73)</td>
</tr>
</tbody>
</table>

* Percent based on K-M estimate (number of subjects with event).
1. Major Adverse Events (MAE) defined as all-cause death, clinically-driven TVR, major target limb amputation, thrombosis at the target lesion site at 60 months. Cumulative incidence based on Kaplan-Meier estimate (number of subject with event).
IN.PACT Global Study
Long-Term All-Cause Mortality in Context

Real-World Study

<table>
<thead>
<tr>
<th>All-Cause Mortality</th>
<th>IC+CLI</th>
<th>N-DM</th>
<th>DM</th>
<th>IC</th>
<th>CLI</th>
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<tr>
<td>5-Year</td>
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<tr>
<td>19.5%*</td>
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<td>10-Year</td>
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IN.PACT Global Study

Austria

UK

Sweden

PAD Epidemiological Studies

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<thead>
<tr>
<th>All-Cause Mortality</th>
<th>IC+CLI</th>
<th>N-DM</th>
<th>DM</th>
<th>IC</th>
<th>CLI</th>
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<tr>
<td>5-Year</td>
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<td>38.0%</td>
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<td>24.5%</td>
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<td>29.0%</td>
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<td>75.0%</td>
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<td>10-Year</td>
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<td>20.0%</td>
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<td>39.8%</td>
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<td>58.0%</td>
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<td>63.0%</td>
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</table>

*Cumulative incidence K-M estimate includes CEC adjudicated deaths, only, and does not include deaths found through additional vital status data collection.

IC = Intermittent Claudication
CLI = Critical Limb Ischemia
N-DM = Non-Diabetes Mellitus
DM = Diabetes Mellitus

1. Presented by Zeller, T. VIVA 2020
3. Heikkila, K et al BJS 2018; 105: 1145–1154
IN.PACT SFA Trial

**Robust Level 1 Evidence**
- Prospective, multicenter EU and US, randomized (2:1), single-blinded trial
- 331 patients enrolled: IN.PACT DCB (n = 220) vs. PTA (n = 111)

**Rigorous and Unbiased**
- Independent and blinded Duplex Ultrasound Core Lab, Angiographic Core Lab, and Clinical Events Committee
- Independent Safety Monitoring Board
- External monitoring with 100% source data verification

**Durability of Outcomes**
- Subjects followed up to 5 years

---

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

* Sponsored by Medtronic plc
IN.PACT SFA Trial
Patency Through the Years

Primary Patency by Kaplan-Meier Analysis

IN.PACT SFA Trial
5-Year Effectiveness: Freedom from Reintervention

All target lesion revascularization events were adjudicated by the independent and blinded Clinical Events Committee.
IN.PACT SFA Trial and IN.PACT Global Study
Long-Term Effectiveness and Safety

Summary Through 5 Years

IN.PACT SFA Trial
is the first, independently adjudicated, blinded, randomized trial to demonstrate superior effectiveness of a DCB through 5 years

The IN.PACT Global Study remains the largest and only reported real-world DCB study with independent CEC adjudication through 5 years

These IN.PACT clinical studies demonstrate long-term effectiveness and safety of the IN.PACT Admiral DCB through 5 years providing a viable solution for the treatment of femoropopliteal disease
Thank You
Additional Strategies, Tools & Techniques for Peripheral Vascular Therapies: A Pre-Recorded Case

Thomas Zeller, MD
Universitäts Herzzentrum Freiburg-Bad Krozingen
Bad Krozingen, Germany
Thomas Zeller to moderate pre-recorded case
MR# 500558
Chocolate™ PTA Balloon Catheter

Pressure Relief Grooves
Uniform Dilation Pillows

Nitinol constraining structure for uniform and atraumatic dilation

TM* third party brands are trademarks of their respective owner.
Thank You
Case Discussion and Key Takeaways
Discussion
Big Data and Paclitaxel Safety: Data Landscape on a Larger Scale

Mortality

2. FDA Executive Summary, Fig. 14: paclitaxel status.
## Drug-Coated Balloon Data Transparency
### IN.PACT Clinical Studies Most Published

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<tr>
<th>Medtronic IN.PACT™ Admiral™ DCB</th>
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Calcium and Lesion Length

References

Drug-Coated Balloon Data Transparency

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LEVANT 2
LEVANT 1
LUTONIX Global
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LUTONIX Safety Meta-analysis

ILLUMENATE US Pivotal
ILLUMENATE EU
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ILLUMENATE EU 2-yr Brodmann M, et al. JACC Cardiovasc Interv 2018;11:2357-64
ILLUMENATE Global
ILLUMENATE First in Human
ILLUMENATE Safety Meta-analysis
ILLUMENATE Safety Grey et al., Circulation. 2019;140:1145–1155
Ranger First in Human
Ranger Global

Drug-Coated Balloon Data Transparency
IN.PACT™ Admiral™ drug-coated PTA balloon catheter

Brief Statement

Indications for Use:
The IN.PACT™ Admiral™ Paclitaxel-coated PTA Balloon Catheter is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of de novo, restenotic, or in-stent restenotic lesions with lengths up to 360 mm in superficial femoral or popliteal arteries with reference vessel diameters of 4-7 mm.

Contraindications
The IN.PACT Admiral DCB is contraindicated for use in:
- Coronary arteries, renal arteries, and supra-aortic/cerebrovascular arteries
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system
- Patients with known allergies or sensitivities to paclitaxel
- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children. It is unknown whether paclitaxel will be excreted in human milk and whether there is a potential for adverse reaction in nursing infants from paclitaxel exposure.

Warnings
- A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients.
- Use the product prior to the Use-by Date specified on the package.
- Contents are supplied sterile. Do not use the product if the inner packaging is damaged or opened.
- Do not use air or any gaseous medium to inflate the balloon. Use only the recommended inflation medium (equal parts contrast medium and saline solution).
- Do not move the guidewire during inflation of the IN.PACT Admiral DCB.
- Do not exceed the rated burst pressure (RBP). The RBP is 14 atm (1419 kPa) for all balloons except the 200 and 250 mm balloons. For the 200 and 250 mm balloons the RBP is 11 atm (1115 kPa). The RBP is based on the results of in vitro testing. Use of pressures higher than RBP may result in a ruptured balloon with possible intimal damage and dissection.
- The safety and effectiveness of using multiple IN.PACT Admiral DCBs with a total drug dosage exceeding 34,854 µg of paclitaxel in a patient has not been clinically evaluated.
IN.PACT™ Admiral™ drug-coated PTA balloon catheter

Brief Statement

Precautions

- This product should only be used by physicians trained in percutaneous transluminal angioplasty (PTA).
- This product is designed for single patient use only. Do not reuse, reprocess, or resterilize this product. Reuse, reprocessing, or resterilization may compromise the structural integrity of the device and/or create a risk of contamination of the device, which could result in patient injury, illness, or death.
- Assess risks and benefits before treating patients with a history of severe reaction to contrast agents.
- The safety and effectiveness of the IN.PACT Admiral DCB used in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure or following treatment failure has not been evaluated.
- The extent of the patient's exposure to the drug coating is directly related to the number of balloons used. Refer to the Instructions for Use (IFU) for details regarding the use of multiple balloons and paclitaxel content.
- The use of this product carries the risks associated with percutaneous transluminal angioplasty, including thrombosis, vascular complications, and/or bleeding events.
- Vessel preparation using only pre-dilatation was studied in the clinical study. Other methods of vessel preparation, such as atherectomy, have not been studied clinically with IN.PACT Admiral DCB.
- This product is not intended for the expansion or delivery of a stent.

Potential Adverse Effects

The potential adverse effects (e.g. complications) associated with the use of the device are: abrupt vessel closure; access site pain; allergic reaction to contrast medium, antiplatelet therapy, or catheter system components (materials, drugs, and excipients); amputation/loss of limb; arrhythmias; arterial aneurysm; arterial thrombosis; arteriovenous (AV) fistula; death; dissection; embolization; fever; hematoma; hemorrhage; hypotension/hypertension; inflammation; ischemia or infarction of tissue/organ; local infection at access site; local or distal embolic events; perforation or rupture of the artery; pseudoaneurysm; renal insufficiency or failure; restenosis of the dilated artery; sepsis or systemic infection; shock; stroke; systemic embolization; vessel spasms or recoil; vessel trauma which requires surgical repair.

Potential complications of peripheral balloon catheterization include, but are not limited to the following: balloon rupture; detachment of a component of the balloon and/or catheter system; failure of the balloon to perform as intended; failure to cross the lesion.

Although systemic effects are not anticipated, potential adverse events that may be unique to the paclitaxel drug coating include, but are not limited to: allergic/immunologic reaction; alopecia; anemia; gastrointestinal symptoms; hematologic dyscrasia (including leucopenia, neutropenia, thrombocytopenia); hepatic enzyme changes; histologic changes in vessel wall, including inflammation, cellular damage, or necrosis; myalgia/arthritis; myelosuppression; peripheral neuropathy.

Refer to the Physician's Desk Reference for more information on the potential adverse effects observed with paclitaxel. There may be other potential adverse effects that are unforeseen at this time.

Please reference appropriate product Instructions for Use for a detailed list of indications, warnings, precautions and potential adverse effects. This content is available electronically at www.manuals.medtronic.com.
HawkOne™ directional atherectomy system
Reference Statement

- **Important Information**: Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

- **Indications for Use**: The HawkOne directional atherectomy system is intended for use in atherectomy of the peripheral vasculature. The HawkOne catheter is indicated for use in conjunction with the SpiderFX™ embolic protection device in the treatment of severely calcified lesions. The HawkOne catheter is NOT intended for use in the coronary, carotid, iliac or renal vasculature.

- **CAUTION**: Federal (USA) law restricts this product for sale by or on the order of a physician.
TurboHawk™ peripheral plaque excision system
Reference Statement

- **Important Information**: Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

- **Indications for Use**: The TurboHawk peripheral plaque excision system is intended for use in the atherectomy of the peripheral vasculature. The TurboHawk catheter is NOT intended for use in the coronary, carotid, iliac, or renal vasculature.

- The TurboHawk catheter is indicated for use in conjunction with the SpiderFX™ embolic protection device in the treatment of severely calcified lesions (LX-C only).

- **CAUTION**: Federal (USA) law restricts this product for sale by or on the order of a physician.
SilverHawk™ peripheral plaque excision system

Reference Statement

- **Important Information:** Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

- **Indications for Use:** The SilverHawk peripheral plaque excision system is intended for use in atherectomy of the peripheral vasculature. The catheter is NOT intended for use in the coronary, carotid, iliac or renal vasculature.

- **CAUTION:** Federal (USA) law restricts this product for sale by or on the order of a physician.
Chocolate™ PTA balloon catheter

Reference Statement

**Important Information:** Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

- **Indications for Use:** The Chocolate PTA balloon catheter is intended for balloon dilatation of lesions in the peripheral vasculature, including the iliac, femoral, ilio-femoral, popliteal, infra-popliteal, and renal arteries.

**CAUTION:** Federal (USA) law restricts this product for sale by or on the order of a physician.
TrailBlazer™ support catheter
Reference Statement

**Important Information:** Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

**Indications for Use:** TrailBlazer support catheter are percutaneous, single lumen catheters designed for use in the peripheral vascular system. TrailBlazer support catheters are intended to guide and support a guide wire during access of the vasculature, allow for wire exchanges and provide a conduit for the delivery of saline solutions or diagnostic contrast agents.

**CAUTION:** Federal (USA) law restricts these devices to sale by or on the order of a physician.
SpiderFX™ embolic protection device

Brief Statement

**Important Information:** Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.

**Indications for Use:**

**Lower Extremity (LE) Interventions**
The SpiderFX embolic protection device is indicated for use as a guidewire and embolic protection system to contain and remove embolic material in conjunction with the TurboHawk™ Peripheral Plaque Excision System, either during standalone procedures or together with PTA and/or stenting, in the treatment of severely calcified lesions in arteries of the lower extremities. The vessel diameter at the filter basket placement site should be between 3.0 mm and 6.0 mm.

**Carotid Interventions**
The SpiderFX embolic protection device is indicated for use as a guidewire and embolic protection system to contain and remove embolic material (thrombus/debris) while performing angioplasty and stenting procedures in carotid arteries. The diameter of the artery at the site of filter basket placement should be between 3.0mm and 7.0mm.

**Saphenous Vein Graft (SVG) Interventions**
The SpiderFX embolic protection device is indicated for use as an embolic protection system to contain and remove embolic material (thrombus/debris). The device also acts as the guidewire while performing percutaneous transluminal coronary angioplasty or stenting procedures in coronary saphenous vein bypass grafts with reference vessel diameters of 3.0 mm to 6.0mm. The safety and effectiveness of this device as an embolic protection system has not been established in the cerebral vasculature.

**CAUTION:** Federal (USA) law restricts this product for sale by or on the order of a physician.