What’s next for IN.PACT DCB in 2019?

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Defining Value and Standard of Care

What Is “Value” in Health Care?

Redefining Health Care
Creating Value-Based Competition on Results

Value = Outcome / Cost

IN.PACT DCB SFA Clinical Program

Robust Adjudicated Series of 1837 Subjects

IN.PACT DCB Clinical Program

RCTs + Pivotal Registration 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

¹. Core lab-adjudicated with clinical events committee oversight (IN.PACT Admiral DCB)
². Clinical events committee oversight (IN.PACT Admiral DCB)
Recent DCB Hot Topics

- In the past six months, there have been new data released from the IN.PACT DCB clinical program
  - IN.PACT SFA 5Y results
  - IN.PACT Japan 3Y results
  - IN.PACT Global 3Y results + sub-analyses (e.g., complex lesions)
  - Total IN.PACT outcomes

- In the past few months, meta-analyses assessing safety with paclitaxel
  - IN.PACT meta-analysis among others
Total IN.PACT Pooled Analyses

The Total IN.PACT™ Drug-Coated Balloon Pooled Analyses: Imaging and Propensity-Matched Cohorts

Mehdi Shishehbor, DO PhD MPH
Heart & Vascular Institute, University Hospitals Cleveland Medical Center and Case Western Reserve University School of Medicine, Cleveland, OH

Mehdi Shishehbor, Thomas Zeller, Michael Jeft, Peter Schneider, John Laird, Osamu Iida, Mahmoud Fazavi, Sehíl Parkh
on behalf of the Total IN.PACT clinical program investigators

tct2018

Total IN.PACT All-Subjects Pooled 1-Year Analysis

Mehdi Shishehbor, DO, PhD, MPH
Heart & Vascular Institute, University Hospitals Cleveland Medical Center and Case Western Reserve University School of Medicine, Cleveland, OH

on behalf of the Total IN.PACT steering committee and clinical program investigators

Presented this past fall 2018 at TCT (San Diego) and VIVA (Las Vegas)
Total IN.PACT Pooled Analyses

This analysis combines all subjects treated with the IN.PACT™ Admiral™ DCB and PTA across two RCT trials and two single arm studies.

- IN.PACT SFA Trial: DCB n=220, PTA n=111
- IN.PACT Japan Trial: DCB n=68, PTA n=32
- IN.PACT China Study: DCB n=143
- IN.PACT Global Study: DCB n=1406

All Subjects (Clinical events committee-adjudicated)
- DCB n=1837
- PTA n=143

Imaging Cohort (Duplex Core lab-adjudicated)
- DCB n=926
- PTA n=143

Propensity-Matched Cohort
- DCB n=466
- PTA n=136

Subjects without duplex core-lab adjudication
- DCB n=911
Total IN.PACT Pooled Analyses

**Total IN.PACT Pooled Analysis Design**

This analysis combines all subjects treated with the IN.PACT™ Admiral™ DCB and PTA across two RCT trials and two single-arm studies.

**Total IN.PACT Imaging Cohort**

*Primary Outcome through 12 Months*

- **Log-rank P < .001**
- **Number at risk**
  - 472 (IN.PACT DCB)
  - 449 (Standard PTA)
  - Log-rank P < .001

**Total IN.PACT Propensity-Matched Cohort**

*Primary Outcome through 12 Months*

- **Log-rank P < .001**
- **Number at risk**
  - 466 (IN.PACT DCB)
  - 433 (Standard PTA)
  - Log-rank P < .001

*Displayed Core lab- and CEC-adjudicated*
Total IN.PACT Pooled Analyses

IN.PACT SFA I & II Trial
DCB n=220
PTA n=111

IN.PACT Japan Trial
DCB n=68
PTA n=32

IN.PACT China Study
DCB n=143

IN.PACT Global Study
DCB n=1406

All Subjects
(Clinical events committee- adjudicated)
DCB n=1837
PTA n=143

12-month Freedom From CD-TLR in Subjects of Standard and Broader Usage

97.1%
91.7%
80.2%

Total IN.PACT All-Subjects Freedom From CD-TLR through 12 months

Log-rank P < .001

Freedom from CD-TLR

Number at risk
1837
1705
1549
143
131
113

DCB Standard Usage

DCB Broader Usage

Standard PTA

Time After Index Procedure (Months)

1125
1028
940

Freedom from CD-TLR

Time After Index Procedure (Months)

Number at risk
712
677
609
143
131
113
IN.PACT DCB Safety

Total IN.PACT Pooled Analysis Initiative

- **IN.PACT SFA I & II Trial**
  - DCB n=220
  - PTA n=111

- **IN.PACT Japan Trial**
  - DCB n=68
  - PTA n=32

- **IN.PACT China Study**
  - DCB n=143

- **IN.PACT Global Study**
  - DCB n=1406

- **All Subjects (Clinical events committee adjudicated)**
  - DCB n=1837
  - PTA n=143

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**IN.PACT Clinical Program: Patient-Level Meta-Analysis**
Mortality Through 5 Years for All DCB vs PTA

<table>
<thead>
<tr>
<th>5-Years</th>
<th>IN.PACT ADMIRAL™ DCB (n = 1697)</th>
<th>PTA (n = 143)</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause Mortality</td>
<td>15.1% (181)</td>
<td>11.2% (16)</td>
<td>0.062</td>
</tr>
</tbody>
</table>

*P-value was from frailty model with study as random effect
Mortality DCB

IN.PACT DCB
Indication Expansions and Approvals??

Fem-Pop US

<table>
<thead>
<tr>
<th>Lutonix 035 (Bard / BD)</th>
<th>IN.PACT Admiral (Medtronic)</th>
<th>Stellarex (Spectranetics / Philips)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Configurations</strong></td>
<td>4.7mm diameter 40-150mm length</td>
<td>4.7mm diameter 40-250mm length</td>
</tr>
<tr>
<td><strong>Platform</strong></td>
<td>Lutonix PTA</td>
<td>Admiral PTA</td>
</tr>
<tr>
<td><strong>Drug and Dosage</strong></td>
<td>Paclitaxel 2.0µg/mm²</td>
<td>Paclitaxel 3.5µg/mm²</td>
</tr>
<tr>
<td><strong>Excipient / Coating</strong></td>
<td>Sorbitol / Polysorbate</td>
<td>Urea</td>
</tr>
<tr>
<td><strong>US Indication</strong></td>
<td>SFA &amp; PA + ISR ≤300mm lesions</td>
<td>SFA &amp; PA + ISR ≤360mm lesions</td>
</tr>
</tbody>
</table>

US indication for IN.PACT DCB for AV access maintenance??

... Waiting for DCB for BTK in US ...
IN.PACT DCB

Indication Expansions and Approvals??

• Global study baseline data were presented by Dr. Lookstein at LINC Leipzig 2019.
• US indication for IN.PACT DCB for AV access maintenance??

IN.PACT AV Access IDE Study Design

• Prospective, global, multicenter, randomized, single-blinded study
• 330 patients
• 24 month follow-up
• 1:1 randomization
• Lesions up to 10 cm in length in the AV Access
• Independent and blinded Duplex Ultrasound Core Lab1, Angiographic Core Lab2, and Clinical Events Committee3
• 30 Global Sites (US, Japan and New Zealand)

IN.PACT AV Access Conclusions

• IN.PACT AV Access IDE Study is evaluating the safety and efficacy of the IN.PACT™ AV Access DCB compared to percutaneous transluminal angioplasty (PTA) for treatment of de-novo or restenotic obstructive lesions of native arteriovenous fistulae (AVF) in the upper extremity
• Subjects from 3 geographies (USA, Japan, NZ) are included
• Anticipating 6-Month Primary results presented in Fall 2019
Defining Value and Standard of Care

How should we be treating our patients? Can we get to an algorithm for managing PAD?

An Algorithm for Drug-eluting Devices:

- **Pre-dilate** (with standard balloon)
  - **Sub-optimal or failed PTA** (calcium, dissection, recoil)
    - Scaffold
  - **Optimal or successful PTA**
    - Drug Coated Balloon
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