Drug-Coated Balloons:

• George S. Chrysant, M.D. FACC, FCSAI, FSCCT
• Chief Scientific Officer
• INTEGRIS Heart Hospital/INTEGRIS Cardiovascular Physicians, LLC
• Oklahoma City, Oklahoma
Disclosures

Consultant:
• Abbott Vascular
• ABIOMED
• Bard
• Boston Scientific
• Medicines Company
• Medtronic
• Spectranetics
• St. Jude Medical
• Toshiba America Medical Systems

Medical/Scientific Boards:
• Abbott Vascular
• Boston Scientific
Further Disclosure

• There are two DCBs currently available in the United States
• Impossible to discuss data without names
Challenging Target Vessels

Lower Extremity Anatomy

- Small arteries - low flow, run-off
- 2 bifurcations (profunda, popliteal)
- Adductor canal
- Common femoral
- Unique vessel forces
- High incidence occlusive disease
- Complex lesions (ostial, calcified)
- High degree of recoil
- Amplified reactivity
- Diffuse nature of disease
DEB treatment strategy

1. PRE-DILATATION
   - Required for all lesions, prior to DCB procedure
   - Standard PTA 1 mm less than reference vessel diameter (RVD)
   - Balloon length should not be greater than the planned DCB length

2. ATERECTOMY
   - Recommended in severely calcified lesions

3. DRUG-COATED BALLOON
   - DCB diameter: RVD = 1:1; length 1 cm beyond lesion on both ends
   - Inflation time $\geq$ 1-3 minutes depending on balloon used
   - Inflation pressure $<$ RBP as required to reach full DCB expansion

4. POST-DILATATION
   - If residual stenosis $\geq$ 50% or flow limiting dissection
   - Standard or high pressure PTA balloon diameter 1:1 to RVD
   - Short / focal length as necessary to treat the extent of residual stenosis or dissection

5. PROVISIONAL SPOT STENTING
   - For persistent residual stenosis $\geq$ 50% or flow limiting dissections
   - Minimum length as necessary to fully treat the residual stenosis or dissection
Provisional stenting rate is dependent on lesion length

Scaffolds still needed but likely at rates proportional to lesion complexity

Provisional stent rates in DCB trials are a function of lesion length

Drug Coated Balloon-PTA
Extensive Development INTO Formulation

The formulation was the result of extensive development and rigorous testing, which included:

- 50,000 balloons
- >11,400 histology samples
- >250 formulations
- 45 preclinical studies

Resulted in an optimized formulation with a therapeutic dose of 2 µg/mm²
Consistent Uniformity  In vivo Delivery

Scientifically designed to:

• Deliver an optimal therapeutic drug dose at the treatment site following a minimum 30-second inflation time*

• Has a consistent coating, resulting in 360º paclitaxel treatment at the target vessel *

• Drug still detectable at 30 days

• Pharmacologic effect out to 90 days

*Animal vessel cross section after 30 sec. inflation*
LEVANT 2 Randomized Study Design

PTA Pre-Dilatation
with 1 mm undersized uncoated balloon
N=487

Successful Pre-Dilation
N=476

Suboptimal PTA:
Major flow limiting dissection or >70% residual stenosis
N=11

Randomization 2:1

Test Arm
DCB
N=316

Control Arm
PTA (POBA)
N=160

Treat Per Standard Practice
30 day follow-up for safety
LEVANT 2 Study Primary Endpoints

Safety

Composite of freedom from all-cause peri-operative death & freedom at 1 YEAR in the index limb from:

• Amputation (ATK or BTK)
• Re-intervention
• Index-limb-related death

Efficacy

Primary patency of the target lesion at 1 YEAR:

• Absence of restenosis defined by DUS PSVR ≥2.5 & freedom from target lesion revascularization (TLR)
In LEVANT 2, 9/10 patients treated with DCB did not require reintervention within a year.
In LEVANT 2, DCB demonstrated a TLR rate consistent with reported SFA stent TLRs*

![Bar Chart](image-url)

**Stent-Like TLR**

- LEVANT 2
- DCB
- TLR rate
- Consistent with SFA stent TLRs

*89.7% Freedom from TLR*
How does IN.PACT Admiral work?

**Mechanism of Action**

The IN.PACT® Admiral® Drug-Coated Balloon Mechanism of Action

Pre-dilatation using an uncoated PTA catheter with a diameter 1 mm less than the reference vessel diameter (RVD) is required prior to use of the IN.PACT Admiral DCB.

This animation is an illustration of the mechanism of action.
The IN.PACT SFA trial provides level 1 clinical data

IN.PACT SFA - 331 Patients
Aggregate dataset from phase I and II

**Primary Endpoints:**
- **Efficacy**: 12 month Primary Patency
- Freedom from clinically-driven TLR and duplex ultrasound derived restenosis (PSVR ≤ 2.4)
- **Safety**: 30 day device / procedure death, 12 month amputation, 12 month clinically-driven TVR

**Key Inclusion Criteria:**
- Rutherford 2-3-4
- SFA and proximal popliteal
- Lesion length 4-18 cm
- Total occlusion ≤ 10 cm
Primary patency is defined as freedom from clinically-driven TLR and freedom from restenosis as determined by duplex ultrasound (DUS) Peak Systolic Velocity Ratio (PSVR) ≤ 2.4.

IN.PACT Admiral primary patency

(p<0.001 by log-rank test)

89.8% IN.PACT

66.8% PTA
Clinically-driven TLR defined as any re-intervention due to symptoms or drop of ABI/TBI of >20% or >0.15 compared to post-procedure ABI/TBI.

Actual event rate by frequency ratio algorithm calculation.

*Qualitative Comparison. Not Meant for Head-to-Head Comparison.
### Efficacy Outcomes (12 Months)

<table>
<thead>
<tr>
<th>Secondary Endpoints</th>
<th>IN.PACT</th>
<th>PTA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD-TLR</td>
<td>2.4% (5/207)</td>
<td>20.6% (22/107)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>All TLR</td>
<td>2.9% (6/207)</td>
<td>20.6% (22/107)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary Sustained Clinical Improvement</td>
<td>85.2% (167/196)</td>
<td>68.9% (73/106)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ABI / TBI</td>
<td>0.951 ± 0.221</td>
<td>0.886 ± 0.169</td>
<td>0.002</td>
</tr>
</tbody>
</table>

### Safety Outcomes (12 Months)

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>IN.PACT</th>
<th>PTA</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Safety Composite</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Device- and Procedure-Related Death (30 Days)</td>
<td>0.0% (0/218)</td>
<td>0.0% (0/111)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Clinically-Driven TVR (12 Months)</td>
<td>4.3% (9/207)</td>
<td>23.4% (25/107)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Target Limb Major Amputation (12 Months)</td>
<td>0.0% (0/207)</td>
<td>0.0% (0/107)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td><strong>Major Adverse Events (12 Months)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-Cause Death</td>
<td>1.9% (4/207)</td>
<td>0.0% (0/107)</td>
<td>0.926</td>
</tr>
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<td>Clinically-Driven TVR</td>
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</tr>
<tr>
<td>Target Limb Major Amputation</td>
<td>0.0% (0/207)</td>
<td>0.0% (0/107)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>1.4% (3/207)</td>
<td>3.7% (4/107)</td>
<td>0.096</td>
</tr>
</tbody>
</table>
Initial Angiogram
Laser Atherectomy
Final Angiogram
DCB: How I use them

- Use in SFA and popliteal
  - Data for BTK controversial to poor

- Make sure prep is pristine
  - Use atherectomy, scoring balloons, cutting balloons
  - 1:1 PTA for prep
  - DCB is for drug application only

- Most useful in ISR

- Both DCBs on the market are very good
  - Give you ~90% 12 month primary patency
  - Cost still an issue
Thank You
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