Towards Standard of Care
DCB-SFA Evidence Status and Outlook

Thomas Zeller, MD
Universitäts-Herzzentrum Freiburg-Bad Krozingen GmbH Bad Krozingen, Germany
Disclosure

Speaker name: Thomas Zeller

I have the following potential conflicts of interest to report:

- Consulting
- Stockholder of a healthcare company

I do not have any potential conflict of interest
Premise: Standard of Care?

- Legal term to position medical best- and mal-practice
- A diagnostic and treatment process that a clinician should follow for a certain type of patient, illness, or clinical circumstance

- An evidence-driven standard built on a proven safety, clinical and cost effective benefit

Premise: Drug Coated Balloons

Rationale and Value

PTA dilatation, short time drug-elution, long term effect

- Restore and maintain patency
- Balloon-type deliverability
- Avoid ISR frequency and burden
- Preserve future options
## The DCB Technology Proliferation

### DCBs (= Drug, ≠ Doses, ≠ Excipients, ≠ Technologies)

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>DCB</th>
<th>Drug</th>
<th>Dose (μg/mm²)</th>
<th>Excipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medtronic</td>
<td>IN.PACT</td>
<td>PTX</td>
<td>3.5</td>
<td>Urea</td>
</tr>
<tr>
<td>BARD</td>
<td>LUTONIX</td>
<td>PTX</td>
<td>2.0</td>
<td>Polysorbate and Sorbitol</td>
</tr>
<tr>
<td>Spectranetics</td>
<td>STELLAREX</td>
<td>PTX</td>
<td>2.0</td>
<td>Polyethylene Glycol</td>
</tr>
<tr>
<td>Biotronik</td>
<td>PASSEO 18 LUX</td>
<td>PTX</td>
<td>3.0</td>
<td>Butyryl-tri-hexyl Citrate</td>
</tr>
<tr>
<td>Cook</td>
<td>ADVANCE 18 PTX</td>
<td>PTX</td>
<td>3.0</td>
<td>none</td>
</tr>
<tr>
<td>Aachen Resonance</td>
<td>ELUTAX</td>
<td>PTX</td>
<td>2.2</td>
<td>dextrane</td>
</tr>
<tr>
<td>Eurocor</td>
<td>FREEWAY</td>
<td>PTX</td>
<td>3.0</td>
<td>shelloic acid</td>
</tr>
<tr>
<td>Cardionovum</td>
<td>LEGFLOW</td>
<td>PTX</td>
<td>3.0</td>
<td>shelloic acid</td>
</tr>
<tr>
<td>Boston Scientific</td>
<td>RANGER</td>
<td>PTX</td>
<td>2.0</td>
<td>citrate ester</td>
</tr>
<tr>
<td>Vascular</td>
<td>LUMINOR</td>
<td>PTX</td>
<td>3.0</td>
<td>unknown</td>
</tr>
<tr>
<td>Biopath</td>
<td>SeQuent Please</td>
<td>PTX</td>
<td>3.0</td>
<td>Iopromide</td>
</tr>
<tr>
<td>Biopath</td>
<td>Biopath</td>
<td>PTX</td>
<td>3.0</td>
<td>Shellac</td>
</tr>
</tbody>
</table>
The DCB Evidence Proliferation

23+ DCB-SFA Peer Reviewed Publications

- **Proof-of-Concept** [1-7]
- **Registries** [8]
- **Pivotal RCTs DCB vs. PTA** [9-10]
- **Retrospective head-head DCB vs. DES** [11]
- **DCB+Stent vs. Stent** [12]
- **DCB in ISR** [13-17]
- **Meta analysis** [18-20]
- **Cost-economic** [21-23]
DCB concept works!

5 DCBs showing a biologic effect

<table>
<thead>
<tr>
<th>DCB</th>
<th>PTX Concentration</th>
<th>Excipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paccocath</td>
<td>3 µg/mm²</td>
<td>Ultravist</td>
</tr>
<tr>
<td>Lutonix</td>
<td>2 µg/mm² + + Polysorbate &amp; Sorbitol</td>
<td></td>
</tr>
<tr>
<td>Passeo 18 Lux</td>
<td>3.0 µg/mm² + + BTHC</td>
<td></td>
</tr>
<tr>
<td>In.Pact</td>
<td>3.5 µg/mm² + + Urea</td>
<td></td>
</tr>
<tr>
<td>Advance PTX</td>
<td>3.0 µg/mm² + + No Excipient</td>
<td></td>
</tr>
<tr>
<td>Stellarex</td>
<td>2.0 µg/mm² + + PEG</td>
<td></td>
</tr>
</tbody>
</table>

6. D.Scheinert – LINC 2013 oral presentation
TASC A-B

~90% and 80% Core-lab adjudicated Primary Patency at 1 and 2-year seen in 2 DCB Trials

IN.PACT SFA
RCT, 220 DCB Patients

ILLUMENATE FIH
single-arm, 50 DCB Patients

LEVANT 2
RCT, 316 DCB Patients

2Y Primary Patency

<table>
<thead>
<tr>
<th></th>
<th>IN.PACT SFA</th>
<th>ILLUMENATE FIH</th>
<th>LEVANT 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>730-day</td>
<td>78.9%</td>
<td>80.3%</td>
<td>56.8%</td>
</tr>
<tr>
<td>760-day</td>
<td>na</td>
<td>80.3%</td>
<td>na</td>
</tr>
</tbody>
</table>

- KM estimates of Duplex derived Primary Patency based on PSVR <2.5
- Duplex Corelab adjudicated (VascCore, Boston, MA, USA)
TASC C-D

Remarkable results seen in long lesions at 1 year

**In.Pact GLOBAL**
(Long Lesion subset)

- N = 164
- Lesion length: 26.40 ± 8.61 cm
- CTO: 60.4%; Ca++: 19.6%

- **1Y Primary Patency:**
  - 91.1% (360d)
  - 80.7% (390d)
  (corelab adjudicated)

- 1-year CI-driven TLR: 6.0%
- Provisional Stenting: 40.4%

**In.Pact LONG**

- N = 105
- Lesion length: 25.17 ± 7.90 cm
- CTO: 49.5%

- **1Y Primary Patency:**
  - 89.3% (360d)
  - 77.2% (390d)
  (corelab adjudicated)

- 1-year CI-driven TLR: 4.0%
- Provisional Stenting: 10.5%

D.Scheinert, oral presentation – EuroPCR 2015

A.Micari, oral presentation – EuroPCR 2015
In Stent Restenosis

DCB better than PTA @ 1 year, (but risk of complete catch-up @ 3 years?)

DEBATE ISR [1]
- N= 44
- 100% DM, 75% CLI
- ISR length = 13.2 cm

FAIR [2]
- RCT DCB vs. PTA
- N= 119
- ISR length = 8.2

DEBATE ISR 3Y [3]


DCB Clinical Evidence Programs

More Evidence to come from structured, comprehensive high quality clinical programs
Cost Effectiveness

TLR ↓↓ makes DCB cost effective for payers in different countries / HC Systems

- DCB and DES cost effective vs. PTA and BMS over a 2-year horizon
- Less “headroom” left for hospitals and facility providers

- DCB carry lowest lifetime costs, highest N of QALYs, highest (~60%) probability to be cost-effective at any “Willingness To Pay” threshold
- DCB is a cost-effective alternative to PTA with bail-out BMS

- DCB may be a cost-saving strategy for payers but carry negative financial impact on providers
- A specific DCB code is needed to satisfy both stakeholders
Lessons learned (1)

- **Geographic miss**: watch out and avoid!
- **Pre-dilatation**: good to assess lesion type, «protect» DCB performance, limit stent use
- **Dissections**: leave it unless flow-limiting
- **Plaque Regression**: higher residual %DS vs. standard PTA is OK
Lessons learned (2)

- **Stenting**: just less needed and still necessary
- **Calcium**: watch out and pre-treat, especially if 360°/Ca++
- **ISR**: DCB good but more needed in occlusive / long diffuse ISRs
- **Combination Therapies**: likely to improve DCB outcomes in complex settings
Conclusions

• Standard of Care: an *evidence* driven path
• Implies a diligent evidence appraisal by physicians and Regulatory Authorities of the Quality of Evidence and Quality of Outcomes
• Few DCBs have shown sound performance and great potential, hence are driving «DCB Therapy» towards *standard of care*
• However not all DCBs are even until they all prove to be even
Towards Standard of Care
DCB-SFA Evidence Status and Outlook

Thomas Zeller, MD
Universitäts-Herzzentrum Freiburg-Bad Krozingen GmbH Bad Krozingen, Germany