Adverse effects of Paclitaxel on arterial pathology:

Are we using the right drug on our DCBs?

Ulrich Beschórrner
Disclosure

Speaker name: Ulrich Beschorner

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☒ I do not have any potential conflict of interest
Paclitaxel can induce adverse vascular pathology and transcriptional responses.

<table>
<thead>
<tr>
<th></th>
<th>TUNEL+ cells (%)</th>
<th>SMC content (%)</th>
<th>Collagen content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Media</td>
<td>Intima</td>
<td>Media</td>
</tr>
<tr>
<td>Control DEC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1% SEC</td>
<td>1.99 (0.68)</td>
<td>0.58 (0.24)</td>
<td>27.5 (2.7)</td>
</tr>
<tr>
<td>2.5% SEC</td>
<td>1.78 (0.77)</td>
<td>0.42 (0.21)</td>
<td>16.9 (2.9)*†</td>
</tr>
<tr>
<td>1% PEC</td>
<td>0.84 (0.79)</td>
<td>0.95 (0.56)</td>
<td>2.6 (0.9)*††</td>
</tr>
<tr>
<td>2.5% PEC</td>
<td>19.2 (5.7)*††‡§</td>
<td>3.1 (3.08)</td>
<td>3.8 (0.9)*††</td>
</tr>
</tbody>
</table>

Values are mean (SEM); n=8/group.

DEC, drug-eluting cuff; IEL, internal elastic lamina; PEC, paclitaxel-eluting cuff; SEC, sirolimus-eluting cuff; SMC, smooth muscle cell.

*p<0.05 vs control DEC; †p<0.05 vs 1% SEC; ‡p<0.05 vs 2.5% SEC; §p<0.05 vs 1% PEC.

IEL disruption was quantified as the number of broken IEL for each cuffed artery segment; medial macrophage content was assessed with a 1–3 score.
Late lumen enlargement after DCB in the coronaries


Bernardo Cortese et al. JCIN 2015;8:2003-2009

Late lumen enlargement after DCB in peripheral arteries

Scheinert, CIRSE, 2016

Werk et al., Circinterventions 2012
Clinical case, 76 y female

SFA-CTO recanalization with DCB (Impact) 2011
still patent 2016

Focal dilatation without aneurysmatic deformation
Can DCB cause dangerous aneurysms?

Only 3 cases in retrospective evaluation of 380 DCB PCI with FU-angio

No accumulated cases within all published studies so far

Combination of DCB with adjunctive therapies?

Kleber, Schulz et. al, Eurointervention 2013
Clinical case, 68 y male

Severe claudication right calf

Duplex: Long occlusion SFA and APOP
Supera 6/100, 6/80, 6/150
1y FU
Clinical case, 78 y female

SFA recanalization with DCB and Stenting 2013
(Inpact, Everflex)
Reocclusions 2014 and 2015

Stents partially exposed after local lysis

Treatment with VIABAHN
Clinical case, 77 y male

6 month FU

APOP Treatment with Turbohawk and DCB DEB 6/100mm

6 month FU
Clinical case, 48 y male

FU
Directional Atherectomy With Antirestenotic Therapy vs Drug-Coated Balloon Angioplasty Alone for Isolated Popliteal Artery Lesions

Konstantinos Stavroulakis, MD1,2, Arne Schwindt, MD1,2, Giovanni Torsello, MD, PhD1,2, Arne Stachmann1,2, Christiane Hericks1,2, Michel J. Bosiers, MD1,2, Efthymios Beropoulis, MD1,2, Stefan Stahlhoff, MD1,2, and Theodosios Bisdas, MD1,2

7% Aneursms
Adverse events of prolonged paclitaxel elution

Aneurysmatic degeneration @ 12 months: N=5 pts (8%)
Potential solution: LIMUS

Aloke Finn, MD
CVPath Institute Inc
In the setting of coronary DES, sirolimus is more effective than paclitaxel in terms of inhibiting proliferation.
<table>
<thead>
<tr>
<th>ATTRIBUTE</th>
<th>LIMUS</th>
<th>PAACLITAXEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of action</td>
<td>Cytostatic</td>
<td>Cytotoxic</td>
</tr>
<tr>
<td>Margin of safety</td>
<td>10,000 fold</td>
<td>100 fold</td>
</tr>
<tr>
<td>Anti-restenosis</td>
<td>Optimal</td>
<td>Good</td>
</tr>
<tr>
<td>Tissue absorption And elution</td>
<td>More difficult</td>
<td>Easier</td>
</tr>
<tr>
<td>Level of competition</td>
<td>Low</td>
<td>Very high</td>
</tr>
<tr>
<td>Physician perception</td>
<td>Positive</td>
<td>Controversial</td>
</tr>
</tbody>
</table>

Source: Oral presentation TCT 2016, P. Stella.
Peripheral FIH – SELUTION SFA

ClinicalTrials.gov ID: NCT02941224

OBJECTIVES
To assess the safety and efficacy of the SELUTION DCB in treatment of de-novo occluded/stenotic or re-occluded/restenotic lesions of SFA and/or PA, assessed at multiple time points clinical, angiographic and/or ultrasound assessment

PRINCIPLE INVESTIGATOR
▶ Thomas Zeller, Bad Krozingen, Germany

DESIGN
▶ Prospective, controlled, multi-center, open, single-arm clinical investigation
▶ 50 patients
▶ 4 centers in Germany

PRIMARY ENDPOINTS
▶ Angiographic Late Lumen Loss (LLL) by QVA – 6 months

SECONDARY ENDPOINTS
▶ Major adverse Events (Death, Thrombosis, Amputation, CD-TLR) 6 months
▶ Primary Patency – Freedom from CD-TLR and absence of Restenosis by DUS - 6, 12 and 24 months
▶ Angiographic Binary Restenosis (ABR) by QVA - 6 months
▶ Composite of Freedom from Amputation and Freedom from CD-TVr – 12 and 24 months
▶ Change of ABI, WIQ and Qol - 6, 12 and 24 months
### Late Lumen Loss

![Late Lumen Loss Chart](chart.png)

### 6-month TLR

![6-month TLR Chart](chart.png)

> Results from different trials are not directly comparable. Information provided for educational purposes.

<table>
<thead>
<tr>
<th>Trial</th>
<th>RANGER SFA</th>
<th>PACIFIER</th>
<th>Tepe et al</th>
<th>LEVANT I</th>
<th>FemPac</th>
<th>BIOLUX-PI</th>
<th>ILLUMENATE</th>
<th>SELUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapy</td>
<td>Ranger</td>
<td>IN.PACT</td>
<td>DCB not</td>
<td>Lutonix</td>
<td>Ptx coated</td>
<td>Passeo-18 Lux</td>
<td>Stellarex</td>
<td>SELUTION</td>
</tr>
<tr>
<td>Mean Lesion Length (mm)</td>
<td>6.8</td>
<td>7.0</td>
<td>5.7</td>
<td>8.1</td>
<td>5.7</td>
<td>6.1</td>
<td>7.2</td>
<td>6.4</td>
</tr>
<tr>
<td>Bailout Stenting (%)</td>
<td>21%</td>
<td>21%</td>
<td>11%</td>
<td>3%</td>
<td>9%</td>
<td>N/A</td>
<td>5%</td>
<td>8%</td>
</tr>
</tbody>
</table>

Are we really using the right drug on our DCBs?

Currently we do not have anything better than Paclitaxel

We should be aware that paclitaxel like any effective drug has side effects

LIMUS coated DCB could be an option in future
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