Drug Coated Balloons: Will They Be Used in All Vascular Beds? Yes or No?

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  - Abbott Medical
  - Alucent Medical
  - SoundBite Medical
  - ROX Medical
  - Zimmer-BioMet

-Royalties/Financial Interest
  - None
- Speaker’s Bureau
  - None
- VIVA Board Member
- I will discuss ‘off-label’ DCB use (outside the US IFU).
Before we get too carried away…

- What is the role of DCB in more complex FPA disease (longer, calcified lesions, CTOs)?
- Where are DCBs a ‘stand alone’ device and where are adjunct technologies required?
- Is the ‘leave nothing behind’ DCB mantra realistic in complex lesions?
- What are the cost implications?
- Are safe and effective DCBs BTK in our future?
It takes considerable knowledge just to realize the extent of your own ignorance.

Thomas Sowell
What Are the Barriers to Expanded DCB Clinical Adoption?

- Despite being a contiguous system, there are considerable ultrastructural, biophysiologic differences between the various vascular beds.
- We CANNOT assume that what works in one vascular bed will work in another vascular bed.
- Understanding drug delivery mechanisms and barriers to absorption is essential to the further development and application of DCBs.
- The confluence of these challenges are likely present in the BTK arteries.
The Anatomy of a Drug Coated Balloon

What are gaps in your knowledge?
Is a balloon the IDEAL PTX Delivery Platform?
Are current PTX/Excipient Platforms Ideal?
How are current DCB iterations addressing current clinical challenges (i.e., Ca++?}

After Granada J in Li et al, Interv Cardiol Clinics 2017
Do We Fully Understand the Pathobiology of Balloon/Vessel Wall Drug Transfer?

Drug coating transfer → Diffusion → Tissue binding → Drug tissue retention

B. Tesfamarian J Controlled Release 2016
Intimal and Medial Calcification: Dual Barriers to Maximal DCB Effect?

Is removal of intimal atheroma alone, not addressing medial calcification, sufficient to maximize PTX effect in complex lesion morphologies?
But wait... We Don’t Even Have a Unified Calcium Grading Scale!

- IN.PACT RTC/Global Japan IP SFA
- ILLUMENATE RCT/ ILLUMENATE Global SFA

**Image Collection**
- >1000 baseline DCB/PTA procedure angiograms
- Patient demographic data

**Core Lab Analysis**
- Core lab uses lesion descriptors and Ca++ as a continuous variable to develop a predictive model
- De-identified referred to stats team

**Statistical Analysis**
- Procedural (≤30d) & CD-TRL thru one-year

**Review & Consensus**
- Determine parameters affecting outcomes
- Proposed definition
- FDA input
- Peer review

**Application**
- Retrospective cohorts
- Ongoing studies
- A future standard for DCB trials ± atherectomy or PTA adjuncts
We Lack an Acceptable In-Vivo Animal to Test Our Hypotheses

Medial calcification was produced in porcine peripheral arteries with similarities to human medial calcification.

Figure 1. External view of the injection sites on day 1.

Figure 2. IVUS image of the injection sites on day 1 (white arrows).

Figure 3. Day 7 post-injection sites on day 1 (white arrows).
Atherectomy Devices: A Partial List

We Need to Assess the Biomechanics of These Adjunct Devices

- These are 510k devices; we need additional (robust) translational and clinical evidence regarding their safety and effectiveness in calcified lesions to drive clinical decision making.
- What is the optimal “vessel preparation” strategy and device?

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Front Cutting</th>
<th>Differential Cutting</th>
<th>Active Aspiration</th>
<th>Concentric Lumens</th>
<th>Lesion Morphology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Soft/Fibrotic Plaque</td>
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<td>✓</td>
<td>✓</td>
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<td>✓</td>
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<tr>
<td>Thrombus</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (indicated for thrombectomy)</td>
</tr>
</tbody>
</table>

DCBs: Understanding the Next Phase of Their Development

US Lutonix IDE enrolls at record pace; Cotavance withdrawn
Bard buys Lutonix for $325M
Cotavance & Moxy FIMs stir interest
FEM PAC THUNDER

Bard/MDT DCBs safe and superior to POBA
IN.PACT Amphirion DEEP withdrawn from market
Biotronik BTK DCB fails to impress
MDT announces EU BTK Pilot
Global registries note limitations of DCBs in complex disease states
CMS limits DCB reimbursement
Bard completes US BTK RTC

Technology Trigger
Peak of Inflated Expectations
Trough of Disillusionment
Slope of Entitlement
Plateau of Productivity
Will DCBs Be Used in All Vascular Beds?

- If there are robust data defining its safety and effectiveness in more ‘real world’ anatomies (longer and calcified arteries)
- IF evaluation of adjuncts to DCB use (atherectomy and boutique balloons) demonstrate clinical safety and effectiveness AND COST EFFECTIVENESS
- If studies demonstrates the safety and effectiveness in BTK lesion in CLI patients
THANK-YOU
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