**BTK DCBs:**
Is Limus the Holy Grail in Light of Prior Failed Trials?

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**Disclosure Statement of Financial Interest**

*Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.*

<table>
<thead>
<tr>
<th>Company</th>
<th>Affiliation/Financial Relationship</th>
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<tbody>
<tr>
<td>Abbott</td>
<td>Consulting Fees / Honoraria</td>
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<td>Boston Scientific</td>
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<td>Medtronic</td>
<td>Consulting Fees / Honoraria</td>
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<td>Penumbra</td>
<td>Honoraria</td>
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BTK DCBs – Is Limus the Holy Grail for BTK Disease?

Challenges to Successful Tibial Intervention:

- Discontinuous AT to DP transition
- Discontinuous PT, with preferential flow in PT from the peroneal

6 Interventions over 2-year period
BTK DCBs – Is Limus the Holy Grail for BTK Disease?

Challenges to Successful Tibial Intervention:

- Flow-limiting dissections
- Residual plaque burden (especially calcified lesions)
- Elastic recoil (immediate, short term)
- Thrombotic occlusion
- Biologic restenosis / intimal hyperplasia
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Drug-Eluting Coronary Stents

- DES shows benefit over BMS/PTA in multiple RCTs
- DES shows best patency results in BTK space and can address acute recoil / residual mechanical burden

12mo Primary patency:

<table>
<thead>
<tr>
<th>Study</th>
<th>DES</th>
<th>BMS/PTA</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACHILLES (vs PTA)</td>
<td>75%</td>
<td>57%</td>
</tr>
<tr>
<td>IDEAS (vs DCB PTA)</td>
<td>72%</td>
<td>42%</td>
</tr>
<tr>
<td>DESTINY (vs BMS)</td>
<td>85%</td>
<td>54%</td>
</tr>
<tr>
<td>YUKON-BTX (vs BMS)</td>
<td>81%</td>
<td>56%</td>
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</table>
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Potential Limitations Permanent Implants in BTK:

- In-stent restenosis
- Re-intervention implications
- Loss of vessel segment as a potential bypass target
- “Stent creep”

We need to meet the challenges posed by tibial disease without impacting future treatment options.
Femoropopliteal DCBs have proven safe and effective in multiple large-scale RCTs.
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Data for DCB vs PTA of Infrapopliteal Lesions

- Several small studies showed benefit for DCB below the knee:
  - DEBELLUM
    - 24.6% BTK disease
    - Improved late lumen loss with DCB (0.66mm vs 1.7mm)
  - DEBATE-BTK
    - 158 BTK; mean lesion length 129mm
    - Lower binary restenosis with DCB (27% vs 74%)
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Amphirion DEEP: failed to meet primary endpoint; amputation trend
Biolux P-II: failed to meet primary endpoint; no safety concerns
Kaplan Meier Efficacy

• 6 months
• DCB 85.3%
• PTA 70.7% (p=0.001)

Primary Safety Endpoint:

• No difference between DCB/PTA at 30 days (p=0.001)

Primary Efficacy Endpoint (patency + limb salvage) @ 6m:

• DCB 73.7%, PTA 63.5% (p=0.0273, NS)
Is Paclitaxel the Right Drug for BTK Disease?

Paclitaxel as Anti-Restenosis Rx

- Proven antiproliferative agent with lipophilic/cytotoxic properties
- Large experience in the peripheral arteries
- Effective on drug-eluting SFA stents
- Effective on DCBs for SFA
- Limited therapeutic window
- Variable efficacy within its therapeutic window(?)
- Has failed in multiple RCTs when used in combination with stents and DCBs in the BTK space, and early generation coronary devices fell out of favor for alternative anti-restenotic therapies
Could Everolimus Be the Right Drug for BTK Disease?

Everolimus as Anti-Restenosis Rx

- Proven antiproliferative agent
- Requires reservoir due to lipophobic/cytostatic properties
- Has wider therapeutic window than PTX
- Also has anti-inflammatory properties
- Has become the established anti-restenotic therapy for coronary arteries, which are more similar to BTK vessels than SFA/pop (at least in diameter)
- Growing evidence exists for use or this drug in the BTK space
### Distinguishing Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Sirolimus</th>
<th>Paclitaxel</th>
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</thead>
<tbody>
<tr>
<td><strong>Mode of Action</strong></td>
<td>Cytostatic</td>
<td>Cytotoxic</td>
</tr>
<tr>
<td><strong>Margin of Safety</strong></td>
<td>10,000 - Fold</td>
<td>100 - Fold</td>
</tr>
<tr>
<td><strong>Therapeutic Range</strong></td>
<td>Wide</td>
<td>Narrow</td>
</tr>
<tr>
<td><strong>Anti-restenotic</strong></td>
<td>Yes (less late lumen loss)</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Anti-inflammatory</strong></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>Tissue Absorption</strong></td>
<td>Slow</td>
<td>Fast</td>
</tr>
<tr>
<td><strong>Tissue Retention</strong></td>
<td>Short</td>
<td>Long</td>
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**BTK DCBs – Is Limus the Holy Grail for BTK Disease?**
BTK DCBs – Is Limus the Holy Grail for BTK Disease?

Limus delivery without a reservoir / depot requires novel mechanism of delivery
BTK DCBs – Is Limus the Holy Grail for BTK Disease?

Sirolimus-Eluting Balloon with Sustained Release

Proprietary MicroReservoir Technology
- Creation of MicroReservoirs combining sirolimus & biodegradable polymer
- Sirolimus - a proven safe & effective cytostatic drug
- Offering a wider therapeutic range

MicroReservoirs: Miniature Drug-Delivery Systems
- Optimal size MicroReservoirs to achieve pharmacokinetic release profile comparable to best in class DES
- Consistent and predictable drug release
- Sustained therapeutic effect for up to 90 days

Cell Adherent Technology (CAT™)
- Proprietary amphipathic lipid technology which binds MicroReservoirs to the balloon surface
  - Contains and protects micro-reservoirs during insertion and inflation
  - Enhances drug retention and bioavailability, allowing for a lower drug dose concentration on the balloon surface (1 μg/mm²)
  - Optimizes transfer of MicroReservoirs to the tissue and maximizes the cellular uptake of sirolimus

1. Drug concentration evident in MicroReservoirs and tissue - Data on File at N.A. Med Alliance SA
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Surmodics SUNDANCE DCB

**Device Specifications**
- Length: 150 cm OTW
- Balloon Diameter: 2.0 – 4.0 mm
- Balloon Length: 20 – 220 mm
- Rated Burst Pressure: 16 ATM
- Minimum Introducer: 5 Fr
- Sirolimus Drug Coating

Holden, A. LINC 2021
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MAGIC TOUCH – Sirolimus Coated Balloon

- MAGICTOUCH® – SCB is Sirolimus Coated Balloon to treat coronary artery disease
- Delivers drug in 60 seconds
- Sub-micron particles
- Supersedes limitations of Paclitaxel

Nothing Leaves Behind

Concept Medical

Slide adapted from Aloeke Finn, MD
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**MAGICAL BTK - IDE FDA**

Sponsored, Prospective, Randomized (2 Magic Touch :1 PTA), multicenter study determine the effectiveness (primary patency) and safety of the sirolimus drug coated balloon (DCB) versus standard percutaneous transluminal angioplasty (PTA) for the treatment of below the knee arterial disease.  

360 Patients

**MAGICAL SFA - IDE FDA**

Sponsored, Prospective, randomized, multi-center study to compare the Magic Touch PTA Sirolimus Coated Balloon with Paclitaxel-coated DCB for treatment of high grade stenotic or occluded lesions in SFA and / or P1 segment of the popliteal artery (PA) in PAD patients.

478 Patients
Conclusions

- The BTK circulation presents specific challenges to successful percutaneous revascularization
- While coronary drug-eluting stents have shown efficacy in small RCTs, these devices have potential negative implications for future open/endovascular interventions
- Paclitaxel-coated DCBs have not shown significant clinical efficacy to date in large randomized clinical trials, and no BTK DCBs are currently approved in the US market
- Limus-based anti-restenotic drugs require novel approaches to drug delivery and tissue uptake, but if these challenges can be overcome they may prove to be more effective than paclitaxel devices due to their unique properties.
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