The Drug-Coated Temporary Spur Stent System*: Innovation in Drug Delivery for Treating CLI

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Disclosures

Speaker name: Jihad A. Mustapha

I have the following potential conflicts of interest to report:
• BD Bard (consultant, physician trainer, research)
• Boston Scientific (consultant, MAB, research)
• Cardio Flow (chief medical officer, board member, shareholder, research)
• Cardiovascular Systems, Inc. (consultant, physician trainer)
• Medtronic (consultant, physician trainer)
• Micromedical Systems (chief medical officer)
• Philips (consultant, physician trainer)
• PQ Bypass (consultant, research)
• Reflow Medical (SAB, research)
• Terumo Medical (consultant & research)
Treatment options for infrapopliteal disease

- **Limb salvage** and mortality rates are comparable in surgical and endovascular interventions\(^1\)

- DCB and DES have improved patency rates, face paclitaxel-related concerns\(^2\)

- **POBA** remains first endovascular choice
  - Unassisted patency rates in 50-60% range

- BMS not shown to be superior

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Anatomical Challenges for DCB and DES Technology BTK

Calcification
- Affects drug uptake
- Affects LLL
- Long term patency decreased

Recoil
- Contributes to restenosis
- Prevalent in patients with diabetes

Drug Uptake Issues
- Diameter mismatch
- Luminal surface contact
- Uptake
- Penetration

Lesion length/tortuosity
- Avg. length: 15-20 cm
- Stents impractical
The Uncoated Temporary Spur Stent System*

- Self-expanding nitinol stent with an integrated balloon
- Deployable and retrievable

- Spur spike* penetrating cadaveric calcium

- Controlled penetration of plaque, calcium, arterial wall, allowing drug uptake.

- Acute luminal gain
  Reduces vessel recoil associated with balloons

- 6 Fr System

- Lesion treated for 2 minutes, followed by DCB for at least two minutes

*For clinical investigational use only; 1. Image courtesy of Prof. Holden, Auckland, NZ
### Clinical Validation: Uncoated Temporary Spur Stent System* with DCB

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Description</th>
<th>Primary Efficacy</th>
<th>Primary Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>DEEPER</td>
<td>Prospective, single center, single arm feasibility study: Spur* + Lutonix DCB.</td>
<td>Primary patency at 6 months (DUS): 88.9% (PP)</td>
<td>Freedom from device and procedure-related death through 30 days: 100% (PP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Completed</td>
<td>Freedom from target limb major amputation and CD-TLR through 6 months: 94.1% (PP)</td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td>DEEPER OUS</td>
<td>Prospective, multicenter (Europe/New Zealand): Spur* + PTx-coated balloon</td>
<td>Primary Efficacy: Primary patency at 6 months (DUS)</td>
<td>Primary Safety: 30-day perioperative mortality</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Enrolling</td>
<td>Vessel Recoil Sub-study: Minimal Lumen Diameter Measurement immediately post-Spur, then 15 minutes post-Spur*</td>
<td></td>
</tr>
<tr>
<td>2020</td>
<td>DEEPER LIMUS</td>
<td>Prospective, single-center (Graz, Austria): Spur* + LIMUS-coated DCB</td>
<td>Primary Safety Endpoint: 6-month composite of All-Cause Mortality, Major Amputation and Clinically Driven Target Lesion Revascularization (CD-TLR)</td>
<td></td>
</tr>
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Drug-Coating Selection

- Concerns for long-term impact of Paclitaxel (Katsanos, et. al., 2018, 2020)
- Limus-based drug coating historically challenging to deliver in absence of stent
- Temporary Spur Stent System*→ Ideal platform for DRUG DELIVERY into diseased artery, may improve tissue absorption and elution

<table>
<thead>
<tr>
<th>ATTRIBUTE</th>
<th>LIMUS</th>
<th>PACLITAXEL</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>

Gaines: Presentation from CRR2019

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# Coating Development

<table>
<thead>
<tr>
<th>DRUG FORMULATION</th>
<th>COATING SYSTEM</th>
</tr>
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<tbody>
<tr>
<td>Sirolimus API and excipient</td>
<td>Stent and balloon coated individually</td>
</tr>
<tr>
<td></td>
<td>Ensures maximum drug: surface area</td>
</tr>
<tr>
<td></td>
<td>Increase uniform drug delivery</td>
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</table>

Drug-coated Temporary Spur Stent System*
How does the Temporary Spur Stent System* Address Common Coating issues?

- Covered design minimizes drug loss to circulation in transit
- Allows uniform and rapid drug deposition directly into arterial wall
  - Reduces surface diffusion of drug
- Nothing left behind
  - Natural anatomical function of the vessel preserved
Drug-Coated Temporary Spur Stent System*

- Drug Coated SPUR System
- Mechanical Piercing of Arterial Wall
  (Scanning Electron Microscope Image)
- Piercing Arterial Layers
- Removal of Coated SPUR Stent
  - Drug remains and penetrates through tissue wall
  (Red dye on tines in animal model)

*Arterial Dye Penetration performed by InnoRA GMBH

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## Next Steps: Randomized Controlled Trial

<table>
<thead>
<tr>
<th>PHASE</th>
<th>ENDPOINTS</th>
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</thead>
<tbody>
<tr>
<td><strong>PHASE A</strong></td>
<td><strong>Safety:</strong> Freedom from the occurrence of major adverse limb events (MALE), and peri-operative death (POD), in Spur and PTA-treated patients through 30 days post-procedure.</td>
</tr>
<tr>
<td>Feasibility: 20 subjects randomized 1:1</td>
<td></td>
</tr>
<tr>
<td><strong>PHASE B</strong></td>
<td><strong>Safety:</strong> Freedom from the occurrence of POD at 30 days, and the occurrence of MALE at 6 months. <strong>Efficacy:</strong> Freedom from a composite endpoint of the occurrence of Major Adverse Events (MAE) at 6 months.</td>
</tr>
<tr>
<td>Pivotal</td>
<td></td>
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- Drug Coated Temporary Spur Stent System* vs PTA
- Dual phase
- Prospective, multicenter, blinded, randomized controlled trial
- Adaptive trial design

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Summary

- Temporary Spur Stent System* **safe** and **promising** novel technology for cardiovascular disease
- Sirolimus drug-coating selected for safety **AND** efficacy
- System received break-through designation November, 2019
- **DEEPER RCT** to commence in 2021
THANK YOU

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