LIMBO: Adventitial Dexamethasone Micro-Infusion to Prevent Restenosis in BTK Arteries

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Disclosure

Speaker name: George Adams, MD

I have the following potential conflicts of interest to report:

- [x] 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
RESTENOSIS

Drug-Eluting Stents

Drug-Coated Balloons

Direct Drug Delivery

DES have shown no improvement in short segment BTK disease

DCB trials have been disappointing (IN.PACT DEEP, BIOLUX P-II)

Direct Drug Delivery may hold promise...
The Bullfrog® Micro-Infusion Device (Mercator MedSystems)
## Background Data from DANCE (Adventitial DEX in SAF/Pop)

### Interim: 73 DANCE Atherectomy Subjects

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rutherford 2</td>
<td>23.3%</td>
</tr>
<tr>
<td>Rutherford 3</td>
<td>61.6%</td>
</tr>
<tr>
<td>Rutherford 4</td>
<td>15.1%</td>
</tr>
<tr>
<td>Severe Calcification</td>
<td>26.6%</td>
</tr>
<tr>
<td>Popliteal Involvement</td>
<td>20.5%</td>
</tr>
<tr>
<td>TASC II Classification</td>
<td>36% A; 59% B; 6% C</td>
</tr>
<tr>
<td>Restenosis</td>
<td>8.2%</td>
</tr>
<tr>
<td>Lesion Length (cm)</td>
<td>8.8 ± 5.2</td>
</tr>
<tr>
<td>%DS (Pre)</td>
<td>69% ± 17%</td>
</tr>
<tr>
<td>Total Occlusions</td>
<td>15.4%</td>
</tr>
<tr>
<td>Grade B-D Dissection</td>
<td>25.0%</td>
</tr>
<tr>
<td>Stent Utilization</td>
<td>34.2%</td>
</tr>
<tr>
<td>%DS (Post)</td>
<td>20% ± 7%</td>
</tr>
</tbody>
</table>

### Safety (0-360 Days)

<table>
<thead>
<tr>
<th>Event</th>
<th>Count (Rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device-related SAE</td>
<td>0/83 (0%)</td>
</tr>
<tr>
<td>Drug-related SAE</td>
<td>0/83 (0%)</td>
</tr>
<tr>
<td>Major Adverse Limb Events</td>
<td></td>
</tr>
<tr>
<td>Amputation</td>
<td>0/83 (0%)</td>
</tr>
<tr>
<td>Bypass</td>
<td>2/83 (2.4%)</td>
</tr>
<tr>
<td>Thrombolysis</td>
<td>0/83 (0%)</td>
</tr>
<tr>
<td>Death 0-30 Days</td>
<td>0/97 (0%)</td>
</tr>
<tr>
<td>Death 0-360 Days</td>
<td>5/88 (5.7%)</td>
</tr>
</tbody>
</table>

### Efficacy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLR at 360 Days</td>
<td>8.3%</td>
</tr>
<tr>
<td>Patency at 360 Days</td>
<td>85.0%</td>
</tr>
<tr>
<td>TLR at 390 Days</td>
<td>8.8%</td>
</tr>
<tr>
<td>Patency at 390 Days</td>
<td>81.5%</td>
</tr>
</tbody>
</table>
LIMBO Trial

**LIMBO-ATX**
- Baseline angiogram and biomarker blood draw
  - 120 ATX (U.S.)
    - 60 controls
    - 60 DEX
  - 24-hour blood draw for $\Delta$ biomarkers
  - 1-month blood draw for $\Delta$ biomarkers
  - Clinical, hemodynamic and angiographic follow-up at 6 months

**LIMBO-PTA**
- 120 PTA (Germany)
  - 60 controls
  - 60 DEX
  - 24-hour blood draw for $\Delta$ biomarkers
  - 1-month blood draw for $\Delta$ biomarkers
  - Clinical, hemodynamic and angiographic follow-up at 6 months
LIMBO Key Eligibility Criteria

• Single or multiple atherosclerotic lesion(s); up to 30 cm in length
• ≥70% diameter stenosis in at least one infra-popliteal target vessel may extend into the distal popliteal (P3)
• Target vessel diameter of ≥2 mm
Primary LIMBO Endpoint - TVAL

TVAL: Transverse-view Vessel Area Loss
A measurement of AREA opacified by contrast, rather than the narrowest cross-section, which LLL defines

LLL = MLD\textsubscript{baseline} - MLD\textsubscript{follow-up} (in mm)

TVA = shaded area within TL end constraints (in mm\textsuperscript{2})
TVAL = 100% - (TVA\textsubscript{f/u} / TVA\textsubscript{baseline})

Courtesy of Kirk Seward, PhD, Mercator MedSystems
LIMBO Secondary Endpoints

• Safety
  – Major adverse limb event and perioperative death (MALE-POD)
  – Clinically driven target lesion revascularization (CD-TLR)
• Effectiveness
  – Patency
  – Wound healing
  – Biomarkers (CRP and MCP-1)
• Healthcare economics
• Technical success
• Revascularization success
Conclusion

• Bullfrog delivery of dexamethasone after atherectomy in SFA and popliteal arteries
  – Reduces production of inflammatory biomarkers versus atherectomy alone
  – Demonstrates adequate patency results of 82.3% at 390 days
• Bullfrog delivery into the BTK vessels is technically feasible
• LIMBO incorporates novel endpoints to the disease state (inflammatory biomarkers) and resulting outcomes (TVAL)
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