Long-term Outcomes for the Ranger Drug-Coated Balloon vs Uncoated Balloons: RANGER II SFA Randomized Trial

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Graz, Austria

on behalf of the RANGER II SFA Investigators
Disclosure

• Speaker name: Marianne Brodmann

• I have the following potential conflicts of interest to report:
  • Consultant: Medtronic, BD BARD, Philipps, Biotronik, Boston Scientific, Cagent, Shockwave, Cook Medical, Bayer Healthcare, Daiichi Sankyo, MedAlliance, Reflow Medical
  • Speakers’ Bureau: Medtronic, BD BARD, Philips, Biotronik, Boston Scientific, Cagent, Shockwave, Cook Medical, Bayer Healthcare, Daiichi Sankyo, MedAlliance, Reflow Medical
# RANGER II SFA Global Study Overview

| Principal Investigators | Global: Prof. Thomas Zeller, MD  
<table>
<thead>
<tr>
<th></th>
<th>United States: Ravish Sachar, MD, FACC</th>
</tr>
</thead>
</table>
| **Study Design**        | **RCT**  
|                         | *(Ranger™ DCB vs Standard PTA)*  
|                         | • 3:1 randomized  
|                         | • Single-blind  
|                         | • Superiority design for effectiveness  
| **Pharmacokinetics Sub-study** | **(Ranger DCB)**  
|                         | • Single-arm  
| **Long Balloon Sub-study** | **(Ranger DCB)**  
|                         | • Single-arm  
| **Patients**            | **N=376**  
|                         | *(Ranger DCB N=278 vs PTA N=98)*  
|                         | • Symptomatic PAD (Rutherford 2-4)  
|                         | • Stenotic lesions of the femoropopliteal segment, up to 180 mm  
|                         | **N=12**  
|                         | **N=52**  
| **Balloon Sizes**       | **Diameter**  
|                         | **Length**  
|                         | **4-8 mm**  
|                         | **30-100 mm**  
| **Investigational Centers** | **United States**  
|                         | **67 study centers: United States, Japan, New Zealand, Europe, Canada**  
|                         | **7 study centers: Belgium, Austria, New Zealand**  

DCB, drug-coated balloon; PAD, peripheral artery disease; PTA, percutaneous transluminal angioplasty; RCT, randomized controlled trial.
Ranger™ Drug Coated Balloon

- Sterling™ Balloon 0.018 inch platform
- 0.014 inch /0.018 inch guidewire compatible
- Size matrix:
  - SFA: 4-8 mm; 30-200 mm
  - BTK: 2-4 mm; up to 150 mm
- TransPax™ coating technology
  - Paclitaxel 2 µg/mm²
- Ranger™ DCB Loading Tool
  - Designed to protect the drug coating and prevent drug loss during insertion
RANGER II SFA RCT
Key Eligibility Criteria

**Inclusion**

- Rutherford classification 2, 3, or 4
- Lesions in the native SFA and/or PPA
- Angiographic evidence for:
  - 70%-99% stenosis with total lesion length up to 180 mm; or
  - Occlusion with total lesion length ≤100 mm
- Reference vessel diameter 4-8 mm

**Exclusion**

- Failure to successfully pre-dilate the target vessel
- Use of adjunctive primary treatment modalities (e.g., debulking devices)
- Previous treatment with stent (i.e., in-stent restenosis) or surgery
- Treatment with atherectomy or a DCB in the past 12 months
- Dialysis
### Demographics and Clinical History

<table>
<thead>
<tr>
<th></th>
<th>Ranger DCB (N=278)</th>
<th>Standard PTA (N=98)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Year)</td>
<td>70.6±9.5</td>
<td>69.1±10.3</td>
<td>0.1887</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>37.8%</td>
<td>31.6%</td>
<td>0.2769</td>
</tr>
<tr>
<td>Smoking History</td>
<td></td>
<td></td>
<td>0.0303</td>
</tr>
<tr>
<td>Current</td>
<td>31.3%</td>
<td>45.9%</td>
<td></td>
</tr>
<tr>
<td>Previous</td>
<td>54.0%</td>
<td>38.8%</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>14.4%</td>
<td>15.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Diabetes Mellitus</strong></td>
<td>42.4%</td>
<td>43.9%</td>
<td>0.8055</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>75.9%</td>
<td>79.6%</td>
<td>0.4561</td>
</tr>
<tr>
<td>Hypertension</td>
<td>90.3%</td>
<td>81.6%</td>
<td>0.0232</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>18.9%</td>
<td>21.4%</td>
<td>0.5893</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>47.5%</td>
<td>44.9%</td>
<td>0.6619</td>
</tr>
<tr>
<td>History of Renal Insufficiency</td>
<td>10.8%</td>
<td>5.2%</td>
<td>0.1004</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation or %. a T-test. b Chi-square test. c Fisher exact test.

## RANGER II SFA RCT | Lesion Characteristics

<table>
<thead>
<tr>
<th>Lesion Characteristics</th>
<th>Ranger DCB (N=278)</th>
<th>Standard PTA (N=98)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length (mm)</td>
<td>82.5±48.9</td>
<td>79.9±49.3</td>
<td>0.6551&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>PACSS Calcification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>35.3%</td>
<td>22.4%</td>
<td>0.0194&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Grade 1</td>
<td>12.6%</td>
<td>14.3%</td>
<td>0.6681&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Grade 2</td>
<td>2.5%</td>
<td>1.0%</td>
<td>0.6860&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Grade 3</td>
<td>36.3%</td>
<td>52.0%</td>
<td>0.0064&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Grade 4</td>
<td>11.5%</td>
<td>10.2%</td>
<td>0.7240&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>% Diameter Stenosis</td>
<td>73.7±16.9</td>
<td>78.2±18.4</td>
<td>0.029&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>100% (Occlusion)</td>
<td>18.3%</td>
<td>29.6%</td>
<td>0.019&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Bailout stenting: **Ranger DCB 5.0% (14/278) & Standard PTA 9.2% (9/98) (p=0.1407<sup>b</sup>)**

Angiographic core lab. PACSS, Peripheral Arterial Calcium Scoring System.

Values are mean ± standard deviation or %. <sup>a</sup>T-test. <sup>b</sup>Chi-square test. <sup>c</sup>Fisher exact test.
Kaplan-Meier curves with standard error. Primary patency based on core-lab assessed duplex ultrasound peak systolic velocity ratio (PSVR) ≤ 2.4 at 36 months in the absence of clinically-driven TLR or bypass of the target lesion. Subjects event-free at 1125 days or later are censored at greater than 1125 days.

**RANGER II SFA RCT | 3-Year Primary Patency Kaplan-Meier Analysis**

- **Primary Patency Rate**

  - **Ranger DCB**: 77.4%
  - **PTA**: 73.5%

  Kaplan-Meier curves with standard error. At risk:
  - Ranger DCB: 278, 272, 252, 211, 159
  - PTA: 98, 91, 76, 71, 59

Log-rank p=0.2555
### 3-Year Primary Patency in Pivotal DCB Trials

<table>
<thead>
<tr>
<th></th>
<th>LEVANT II (N=476)</th>
<th>ILLUMINATE (N=300)</th>
<th>IN.PACT SFA (N=331)</th>
<th>RANGER II SFA (N=376)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N</strong></td>
<td>PTA</td>
<td>DCB</td>
<td>PTA</td>
<td>DCB</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>160</td>
<td>316</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td>Occlusions</td>
<td>63.2</td>
<td>62.7</td>
<td>89.0</td>
<td>80.0</td>
</tr>
<tr>
<td>Severe Calcification</td>
<td>21.9%</td>
<td>20.6%</td>
<td>18%</td>
<td>19%</td>
</tr>
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**Primary Patency Rate**

- **LEVANT II (N=476)**
  - Standard PTA: 64.2%
  - Lutonix™ Drug-Coated Balloon (BD): 51.0%
- **ILLUMINATE (N=300)**
  - Standard PTA: 69.5%
  - Stellarex Drug-Coated Balloon (Philips): 45.1%
- **IN.PACT SFA (N=331)**
  - Standard PTA: Not reported
  - IN.PACT™ Admiral Drug-Coated Balloon (Medtronic): 73.5%
- **RANGER II SFA (N=376)**
  - Standard PTA: 77.4%
  - Ranger™ Drug-Coated Balloon (Boston Scientific): 77.4%

**Primary Patency estimates reported in Kaplan-Meier analysis at 1095 days (36 months).**

Results from different clinical investigations are not directly comparable. Information provided for educational purposes only. All trademarks are the property of their respective owners.  

RANGER II SFA RCT | 4-Year Mortality & Major Amputations

- No significant difference in all-cause mortality rates
- No major target limb amputations

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<td>All-Cause Death\textsuperscript{b}</td>
<td>14.0% (39/278)</td>
<td>12.2% (12/98)</td>
<td>0.6574</td>
</tr>
<tr>
<td>Major Target Limb Amputation</td>
<td>0.0%</td>
<td>0.0%</td>
<td>Undef</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Chi-square test.
\textsuperscript{b}Crude rate including all vital status assessments regardless of Clinical Event Committee adjudication.
RANGER II SFA RCT | 4-Year Freedom from CD-TLR
Kaplan-Meier Analysis

Kaplan-Meier curves with standard error.

At risk:
- Ranger DCB
- PTA

Log-rank p=0.2108

- Ranger DCB: 78.7%
- PTA: 74.5%
4-Year Freedom from CD-TLR Rates in Pivotal DCB Trials

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<td>18%</td>
<td>19%</td>
</tr>
<tr>
<td>Severe Calcification</td>
<td>8.1%</td>
<td>10.4%</td>
<td>43.0%</td>
<td>43.9%</td>
</tr>
</tbody>
</table>

Freedom from CD-TLR

- Lutonix Drug-Coated Balloon PTA Catheter (BD): 71.0%
- Stellarex Drug-Coated Balloon (Philips): 76.7%
- IN.PACT Admiral Drug-Coated Balloon (Medtronic): 71%
- Ranger Drug-Coated Balloon (Boston Scientific): 78.7%
- Not reported

Estimates of freedom from CD-TLR reported at 48 months from Kaplan-Meier analyses. Results from different clinical investigations are not directly comparable. Information provided for educational purposes only. All trademarks are the property of their respective owners.

RANGER II SFA RCT | Conclusions
Long-term Follow up

• Similar safety for Ranger DCB and PTA through 4 years
  • No mortality signal

• Demonstrates 3-year primary patency ~77% for low-dose paclitaxel Ranger DCB

• The 3-year primary patency and 4-year freedom from CD-TLR rates for the Ranger DCB group in this study are greater than those reported for other DCBs in previously published pivotal trials
Long-term Outcomes for the Ranger Drug-Coated Balloon vs Uncoated Balloons: RANGER II SFA Randomized Trial

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on behalf of the RANGER II SFA Investigators