Twelve-month Results from the First-in-Human Randomized Study of the Ranger Paclitaxel-Coated Balloon

Gunnar Tepe, MD
RoMed Clinics Rosenheim, Germany
on behalf of the RANGER SFA investigators
Disclosures

Study support:

BBraun, Biotronik, Boston Scientific, CR Bard, Gore, Medtronic/Covidien, TriReme Medical
# RANGER SFA Study Overview

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Dierk Scheinert, MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Sponsor</td>
<td>Hemoteq AG (Würselen, Germany)</td>
</tr>
<tr>
<td><strong>Objective</strong></td>
<td>To prove the superior performance of the Ranger™ paclitaxel-coated PTA balloon catheter (Boston Scientific) for angioplasty for femoropopliteal artery lesions when compared to non-coated balloons at six months post-procedure when comparing Late Lumen Loss (LLL).</td>
</tr>
<tr>
<td><strong>Study Design</strong></td>
<td>Prospective, multicenter, randomized, controlled trial (2:1 Ranger DCB vs. non-drug-coated balloon). Follow up through 3 years.</td>
</tr>
<tr>
<td><strong>Subjects</strong></td>
<td>105 patients with femoropopliteal artery lesions (Rutherford 2-4, lesion length 20 mm - 150 mm)</td>
</tr>
<tr>
<td><strong>Investigational Centers</strong></td>
<td>10 sites (Germany, France, and Austria)</td>
</tr>
</tbody>
</table>
| **Endpoints**           | **Primary:** In-segment late lumen loss of the treated segment, as observed by angiography at 6 months post-procedure  
**Secondary:** Restenosis and patency rates  
Rutherford classification / clinical success  
Ankle-brachial index / hemodynamic success  
Quality of life (WIQ, EQ5D, SF12) |
Patient Enrollment & Follow-up

- 105 patients treated at 10 study centers

1. Assessed for eligibility (N=131)
   - Excluded
     - Not meeting inclusion criteria (n=26)

2. Enrolled and randomized (N=105)

3. Control (N=34)
   - Died n=1
     - Missed visit n=1
   - Withdrew n=2
     - Missed visit n=6
     - Evaluable angiography n=19

4. Ranger DCB (N=71)
   - Withdrew n=2
   - Missed visit n=6
   - Evaluable angiography n=47

5. 6-month follow-up visit completed (n=25)
   - Missed visit n=6
   - Evaluable angiography n=19
   - Withdrew n=2

6. 12-month follow-up visit completed (n=28)
   - Missed visit n=1

7. 12-month follow-up visit completed (n=59)
   - Missed visit n=7

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*Enrollment occurred after successful intraluminal guidewire crossing of the target lesion*
Ranger™ Paclitaxel-Coated PTA Balloon Catheter

- Sterling™ PTA balloon platform
- TransPax™ coating technology
- Paclitaxel: 2 µg/mm² dose density
- Ranger™ DCB Loading Tool
  - Designed to protect the drug coating
- Sizes available for the RANGER SFA study:
  - 4-7 mm diameter; 40-100 mm length

DCB, drug-coated balloon; PTA, percutaneous transluminal angioplasty; SFA, superficial femoral artery
Baseline clinical characteristics similar between Ranger and control groups

<table>
<thead>
<tr>
<th></th>
<th>Control (N=34)</th>
<th>Ranger DCB (N=71)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y (mean±SD)</td>
<td>67 ± 9.4</td>
<td>68 ± 8</td>
<td>0.999</td>
</tr>
<tr>
<td>Men</td>
<td>68%</td>
<td>75%</td>
<td>0.6048</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>35%</td>
<td>39%</td>
<td>0.9336</td>
</tr>
<tr>
<td>COPD</td>
<td>15%</td>
<td>11%</td>
<td>0.8541</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>62%</td>
<td>69%</td>
<td>0.6057</td>
</tr>
<tr>
<td>Hypertension</td>
<td>76%</td>
<td>82%</td>
<td>0.6100</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>50%</td>
<td>41%</td>
<td>0.0217</td>
</tr>
<tr>
<td>Previous</td>
<td>21%</td>
<td>45%</td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>2.9%</td>
<td>5.6%</td>
<td>0.9844</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>38%</td>
<td>34%</td>
<td>0.8207</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>15%</td>
<td>14%</td>
<td>1.0000</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>2.9%</td>
<td>9.9%</td>
<td>0.3816</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>2.9%</td>
<td>11%</td>
<td>0.2920</td>
</tr>
</tbody>
</table>

RANGER SFA
Baseline Lesion Characteristics

Angiographic Core Lab

- Similar lesion characteristics between Ranger and control groups

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<thead>
<tr>
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<th>Control (N=34)</th>
<th>Ranger DCB (N=71)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>60 ± 48</td>
<td>68 ± 46</td>
<td>0.7314</td>
</tr>
<tr>
<td>Total occlusion</td>
<td>34%</td>
<td>34%</td>
<td>1.0000</td>
</tr>
<tr>
<td>Calcification</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>16%</td>
<td>10%</td>
<td>0.2359</td>
</tr>
<tr>
<td>Mild</td>
<td>28%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>34%</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>22%</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal SFA</td>
<td>6%</td>
<td>17%</td>
<td>0.2885</td>
</tr>
<tr>
<td>Middle SFA</td>
<td>38%</td>
<td>44%</td>
<td></td>
</tr>
<tr>
<td>Distal SFA</td>
<td>53%</td>
<td>36%</td>
<td></td>
</tr>
<tr>
<td>Proximal popliteal</td>
<td>3%</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>TASC II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>69%</td>
<td>66%</td>
<td>0.6196</td>
</tr>
<tr>
<td>B</td>
<td>22%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>6%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>0.0%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>% Diameter stenosis</td>
<td>82 ± 18</td>
<td>85 ± 15</td>
<td>0.5740</td>
</tr>
<tr>
<td>Reference vessel diameter</td>
<td>4.5 ± 0.83</td>
<td>5 ± 0.89</td>
<td>0.0389</td>
</tr>
</tbody>
</table>
Primary Efficacy Endpoint - 6 Months
Late Lumen Loss

- LLL was significantly less for Ranger DCB than for control ($P=.0017$)
Primary Patency - 12 Months

Kaplan-Meier Estimate

- KM estimate of primary patency rate at 12 months: 86%
  Ranger DCB vs 56% Control

- Significantly greater time to failure (survival time) for Ranger DCB than control (log-rank $P<.001$)

Primary patency defined as the percentage of lesions without a hemodynamically significant stenosis on duplex ultrasound (PSVR > 2.4) and without TLR or bypass of the target lesion.
Safety Summary - 12 Months

- Significantly lower TLR rate for Ranger DCB than control (P=0.030)
- No target limb amputations
- 3 deaths by 1 year of follow up (1 control, 2 Ranger group). None related to the device or procedure
- Similar AE and SAE rates between groups (P > 0.05)
- No USADE reported

<table>
<thead>
<tr>
<th></th>
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<th>Ranger DCB</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target limb amputation</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Related death</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>TLR</td>
<td>26% (9/34)</td>
<td>8.5% (6/71)</td>
<td>.030</td>
</tr>
</tbody>
</table>

AE, adverse event; SAE, serious adverse event; USADE, unanticipated serious adverse device effects; TLR, target lesion revascularization
Freedom from TLR

Kaplan-Meier Estimate

- KM estimate of freedom from TLR at 12 months: **91%**
  - **Ranger DCB** vs **70% Control**

- Significantly greater TLR-free time for Ranger DCB than control (log-rank $P=.010$)

**At risk:**

<table>
<thead>
<tr>
<th></th>
<th>Ranger DCB</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since procedure (days)</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>69</td>
<td>31</td>
</tr>
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TLR, target lesion revascularization
Clinical Outcomes

Rutherford Classification

- 84% of subjects in the Ranger DCB group presented with no or mild symptoms (category 0-1) at 12-month follow-up
- Distributions for both Control and Ranger DCB groups show a shift to lower Rutherford Categories ($P<.05$)
  - Not significantly different between groups

<table>
<thead>
<tr>
<th>Rutherford Classification</th>
<th>Baseline (n=34)</th>
<th>6 Months (n=26)</th>
<th>12 Months (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asymptomatic</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Claudication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Critical Limb Ischemia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
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Control

- 68% of subjects in the Control group presented with no or mild symptoms (category 0-1) at 12-month follow-up

Ranger DCB

- 94% of subjects in the Ranger DCB group presented with no or mild symptoms (category 0-1) at 12-month follow-up

RANGER SFA
Clinical Outcomes

ABI/Hemodynamic Success
- Significant improvement in ABI in both groups at 12 months ($P<.05$)
- Hemodynamic success rate (positive ABI change ≥0.1) was 81.2% for Ranger DCB and 70.4% for Control ($P=.4278$)

Walking Function and Quality of Life
- No significant differences between groups for WIQ, EQ5D, or SF12

ABI, ankle-brachial index; WIQ, Walking Impairment Questionnaire
Conclusions

• Greater patency rate at 12 months for Ranger DCB than Control (KM estimate: 86% vs 56%)

• Freedom from TLR greater for Ranger DCB than Control at 12 months (KM estimate: 91% vs 70%)

• Patients treated with Ranger DCB demonstrated significant improvements in symptoms and hemodynamics at 12 months
  o Symptomatic improvement generally similar to Control but with ~1/3 as many revascularizations