New insights from Ranger DCB in challenging lesions and demographics

Marianne Brodmann, MD
Medical University Graz
Graz, Austria
IMPORTANT INFORMATION: These materials are intended to describe common clinical considerations and procedural steps for the on-label use of referenced technologies as well as current standards of care for certain conditions. Of course, patients and their medical circumstances vary, so the clinical considerations and procedural steps described may not be appropriate for every patient or case. As always, decisions surrounding patient care depend on the physician’s professional judgment in light of all available information for the case at hand.

Boston Scientific Corporation (“BSC”) does not promote or encourage the use of its devices outside their approved labeling.

The presenter’s experience with BSC products may not be interpreted or relied upon to support clinical claims about BSC devices or product comparison claims regarding BSC and competitive devices. The experiences of other users may vary.

Results from case studies are not necessarily predictive of results in other cases. Results in other cases may vary.
Disclosures

• Consultant: BD BARD, Philips, Medtronic, Bayer Healthcare, Cagent, Surmodics, Biotronik, iVascular, Boston Scientific, Abbot, Shockwave, Intact Vascular

• Speakers’ Bureau - BD BARD, Philips, Medtronic, Bayer Healthcare, Cagent, Surmodics, Biotronik, iVascular, Boston Scientific, Abbot, Shockwave, Intact Vascular
## RANGER II SFA Global Study Overview

### Principal Investigators
- **Global:** Prof. Thomas Zeller, MD
- **United States:** Ravish Sachar, MD, FACC

### Study Design
<table>
<thead>
<tr>
<th>Study Design</th>
<th>RCT (Ranger™ DCB vs Standard PTA)</th>
<th>Pharmacokinetics Sub-study (Ranger DCB)</th>
<th>Long Balloon Sub-study (Ranger DCB)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td><strong>N=376</strong></td>
<td><strong>N=12</strong></td>
<td><strong>N=52</strong></td>
</tr>
<tr>
<td></td>
<td>(Ranger DCB N=278 vs PTA N=98)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Symptomatic PAD (Rutherford 2-4)</td>
<td>• Symptomatic PAD (Rutherford 2-4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Stenotic lesions of the femoropopliteal segment, <strong>up to 180 mm</strong></td>
<td>• Stenotic lesions of the femoropopliteal segment, <strong>up to 180 mm</strong></td>
<td></td>
</tr>
</tbody>
</table>

### Balloon Sizes
<table>
<thead>
<tr>
<th>Balloon Sizes</th>
<th>Diameter</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4-8 mm</td>
<td>30-100 mm</td>
</tr>
</tbody>
</table>

### Investigational Centers
- **67 study centers:** United States, Japan, New Zealand, Europe, Canada
- **United States**
- **7 study centers:** Belgium, Austria, New Zealand
Ranger™ Drug Coated Balloon

- Next generation 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
  - Provides best in class coating integrity
- Ranger™ DCB Loading Tool
  - Designed to protect the drug coating and prevent drug loss during insertion
# RANGER II SFA Global Study Overview

## Principal Investigators
- Global: Prof. Thomas Zeller, MD
- United States: Ravish Sachar, MD, FACC

## Study Design
<table>
<thead>
<tr>
<th>RCT</th>
<th>Pharmacokinetics Sub-study</th>
<th>Long Balloon Sub-study</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Ranger™ DCB vs Standard PTA)</td>
<td>Single-arm</td>
<td>Single-arm</td>
</tr>
<tr>
<td>• 3:1 randomized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Single-blind</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Superiority design for effectiveness</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Patients
<table>
<thead>
<tr>
<th>Patients</th>
<th>N=376 (Ranger DCB N=278 vs PTA N=98)</th>
<th>N=12</th>
<th>N=52</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptomatic PAD (Rutherford 2-4)</td>
<td>Symptomatic PAD (Rutherford 2-4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenotic lesions of the femoropopliteal segment, up to 180 mm</td>
<td>Stenotic lesions of the femoropopliteal segment, up to 180 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion up to 150 mm</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Balloon Sizes
<table>
<thead>
<tr>
<th>Balloon Sizes</th>
<th>Diameter</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4-8 mm</td>
<td>30-100 mm</td>
</tr>
<tr>
<td></td>
<td>4-7 mm</td>
<td>120-200 mm</td>
</tr>
</tbody>
</table>

## Investigational Centers
<table>
<thead>
<tr>
<th>Investigational Centers</th>
<th>United States</th>
<th>7 study centers: Belgium, Austria, New Zealand</th>
</tr>
</thead>
<tbody>
<tr>
<td>67 study centers: United States, Japan, New Zealand, Europe, Canada</td>
<td>United States</td>
<td></td>
</tr>
<tr>
<td>7 study centers: Belgium, Austria, New Zealand</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

**Note:** The provided information is a summary of the study design and patient selection criteria. For detailed information, please refer to the original study documentation.
RANGER II SFA 
Pharmacokinetics Sub-Study

• All patients treated with Ranger DCB (N=12)
• Treated lesion length 154.2±92.8 mm
• Plasma paclitaxel less than the limit of quantification (<1 ng/mL):
  – 11 of 12 patients by 1 hour following DCB deployment and removal
  – all patients by 3 hours
• 1 death, non-cardiovascular, 79 days post-procedure

Protocol required blood draws: baseline, 10 minutes, 30 minutes, 1, 3, 6, 24 or 48 hours, 7 days and 30 days after last Ranger DCB treatment and removal.
**RANGER II SFA Global Study Overview**

| Principal Investigators | Global: Prof. Thomas Zeller, MD  
| United States: Ravish Sachar, MD, FACC |

| Study Design | RCT  
| (Ranger™ DCB vs Standard PTA) | Pharmacokinetics Sub-study  
| (Ranger DCB) | Long Balloon Sub-study  
| (Ranger DCB) |
|---|---|---|
| • 3:1 randomized  
| • Single-blind  
| • Superiority design for effectiveness | • Single-arm | • Single-arm |

| Patients | N=376  
<table>
<thead>
<tr>
<th>(Ranger DCB N=278 vs PTA N=98)</th>
<th>N=12</th>
<th>N=52</th>
</tr>
</thead>
</table>
| • Symptomatic PAD (Rutherford 2-4)  
| • Stenotic lesions of the femoropopliteal segment, **up to 180 mm** | • Symptomatic PAD (Rutherford 2-4)  
| • Stenotic lesions of the femoropopliteal segment, **up to 180 mm**  
| • Occlusion up to 150 mm |

| Balloon Sizes | Diameter  
| Length | 4-8 mm  
| 30-100 mm | 4-7 mm  
| 120-200 mm |

| Investigational Centers | 67 study centers: United States, Japan, New Zealand, Europe, Canada  
| United States  
| 7 study centers: Belgium, Austria, New Zealand |
RANGER II SFA RCT
1-Year Safety Data

- Primary safety endpoint met (non-inferiority P<0.0001)
- 12-month MAE-free rate

94.1% (241/256) Ranger DCB vs 83.5% (76/91) PTA; P=0.002

- Significantly lower MAE and TLR rates for Ranger DCB vs PTA

<table>
<thead>
<tr>
<th>MAE Category</th>
<th>Ranger DCB (N=256)</th>
<th>Standard PTA (N=91)</th>
<th>Difference [95% CI]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>12-Month MAE</strong></td>
<td>5.9% (15/256)</td>
<td>16.5% (15/91)</td>
<td>-10.6% [-18.8%, -2.5%]</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>All Causes of Death at 1 Month</strong></td>
<td>0.4% (1/256)</td>
<td>0.0% (0/91)</td>
<td>0.4% [-0.4%, 1.2%]</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td><strong>Target Limb Major Amputation</strong></td>
<td>0.0% (0/256)</td>
<td>0.0% (0/91)</td>
<td>0.0% [NA, NA]</td>
<td>Undef</td>
</tr>
<tr>
<td><strong>Clinically-Driven TLR</strong></td>
<td>5.5% (14/256)</td>
<td>16.5% (15/91)</td>
<td>-11.0% [-19.1%, -2.9%]</td>
<td>0.001</td>
</tr>
</tbody>
</table>

PTA: Percutaneous transluminal angioplasty; DCB: Drug-coated balloon; MAE: major adverse events; TLR: target lesion revascularization; CI: confidence interval

MAEs were adjudicated by a Clinical Events Committee.
RANGER II SFA RCT
Primary Patency at 12 Months: Full Cohort

Kaplan-Meier Analysis

Log rank P=0.0005

At risk: Ranger DCB
0% 20% 40% 60% 80% 100%
0 2 4 6 8 10 12 14
Months Since Procedure

Ranger DCB 89.8%
Standard PTA 74.0%

Error bars are SE.

PTA: Percutaneous transluminal angioplasty; DCB: Drug-coated balloon
**RANGER II SFA RCT**  
Clinical Outcomes at 12 Months

<table>
<thead>
<tr>
<th>Primary sustained clinical improvement(^a)</th>
<th>Ranger DCB</th>
<th>Standard PTA</th>
<th>Difference</th>
<th>95%CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>87.6% (220/251)</td>
<td>75.8% (69/91)</td>
<td>11.8%</td>
<td>2.1%, 21.5%</td>
<td>0.0076</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Improvement in Rutherford classification of one or more categories as compared to baseline without TLR.

- No or minimal symptoms (Rutherford Category 0-1) at 12 months
  - 85.7% Ranger DCB
  - 74.7% PTA

---

PTA: Percutaneous transluminal angioplasty; DCB: Drug-coated balloon; TLF: total lesion revascularization

# Baseline Characteristics I Ranger DCB

## Women & Men

<table>
<thead>
<tr>
<th>Demographics &amp; Clinical History</th>
<th>Women (n=105)</th>
<th>Men (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>70.6±9.7</td>
<td>70.7±9.3</td>
</tr>
<tr>
<td>Smoking</td>
<td>71.4%</td>
<td>93.6%</td>
</tr>
<tr>
<td>Medically-Treated Diabetes</td>
<td>40.0%</td>
<td>39.9%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89.5%</td>
<td>90.8%</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>41.7%</td>
<td>50.9%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TASC II Type (Site-Reported)</th>
<th>Women (n=105)</th>
<th>Men (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>54.3%</td>
<td>45.1%</td>
</tr>
<tr>
<td>B</td>
<td>20.0%</td>
<td>39.3%</td>
</tr>
<tr>
<td>C</td>
<td>11.4%</td>
<td>9.2%</td>
</tr>
<tr>
<td>D</td>
<td>1.0%</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Core Lab Measurements</th>
<th>Women (n=105)</th>
<th>Men (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length (mm)</td>
<td>75.8±53.2</td>
<td>86.6±45.7</td>
</tr>
<tr>
<td>RVD (mm)</td>
<td>4.7±0.8</td>
<td>5.4±0.8</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>1.3±0.8</td>
<td>1.4±1.0</td>
</tr>
<tr>
<td>% Diameter Stenosis</td>
<td>73.8±15.7</td>
<td>73.7±17.6</td>
</tr>
</tbody>
</table>
Safety I Ranger DCB
Women & Men

• 12-month MAE-free rate:
  93.7% (89/95) Women & 94.4% (152/161) Men
• All MAE were clinically-driven TLRs. Similar rates for women and men treated with Ranger DCB

<table>
<thead>
<tr>
<th></th>
<th>Women (n=105)</th>
<th>Men (n=173)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-Month MAE</td>
<td>6.3% (6/95)</td>
<td>5.6% (9/161)</td>
</tr>
<tr>
<td>All-Cause Death at 1 Month</td>
<td>0.0% (0/95)</td>
<td>0.6% (1/161)</td>
</tr>
<tr>
<td>Target Limb Major Amputation</td>
<td>0.0% (0/95)</td>
<td>0.0% (0/161)</td>
</tr>
<tr>
<td>Target Lesion Revascularization</td>
<td>6.3% (6/95)</td>
<td>5.0% (8/161)</td>
</tr>
<tr>
<td>Clinically-Driven</td>
<td>6.3% (6/95)</td>
<td>5.0% (8/161)</td>
</tr>
</tbody>
</table>

MAEs were adjudicated by a Clinical Events Committee.
Effectiveness I Primary Patency

Among patients treated with Ranger DCB, **no difference** for women vs men

- **Ranger DCB**
  - Women vs Men
- **Log rank p=0.5279**

Among women, **significantly better primary patency** for patients treated with Ranger DCB vs Standard PTA

- **Women**
  - **Ranger DCB vs PTA**
- **Log rank p=0.0084**

Kaplan-Meier estimates with standard errors.

- Primary patency KM estimate utilizing time-to-event of TLR up to 365 days and duplex ultrasound data at 12 months.

Lesion length
- 82.2±62.5 mm
- Diabetes 41.9%
- %DS 77.9%±18.7%

Keirse K, LINC 2021
Freedom from TLR

Ranger DCB
Women vs Men

Among patients treated with Ranger DCB, no difference for women vs men

Log rank p=0.6875

Men 94.9%
Women 93.7%

Women
Ranger DCB vs PTA

Among women, significantly better freedom from TLR for patients treated with Ranger DCB vs Standard PTA

Log rank p=0.0032

Ranger DCB 93.7%
Standard PTA 76.4%

Lesion length 82.2±62.5 mm
Diabetes 41.9%
%DS 77.9%±18.7%

Men
Women

At risk:

105 105
173 31
169 102
161 29
94 94

0 2 4 6 8 10 12
Months Since Procedure

0% 20% 40% 60% 80% 100%

At risk:

Kaplan-Meier estimates with standard errors.

Keirse K, LINC 2021
# RANGER II SFA Global Study Overview

| Principal Investigators | Global: Prof. Thomas Zeller, MD  
United States: Ravish Sachar, MD, FACC |
|-------------------------|----------------------------------------|
| Study Design            | **RCT**  
(Ranger™ DCB vs Standard PTA)  
**Pharmacokinetics Sub-study**  
(Ranger DCB)  
**Long Balloon Sub-study**  
(Ranger DCB) |
|                         | • 3:1 randomized  
• Single-blind  
• Superiority design for effectiveness  
• Single-arm  
• Single-arm |
| Patients                | N=376  
(Ranger DCB N=278 vs PTA N=98)  
N=12  
N=52 |
|                         | • Symptomatic PAD (Rutherford 2-4)  
• Stenotic lesions of the femoropopliteal segment, **up to 180 mm**  
• Symptomatic PAD (Rutherford 2-4)  
• Stenotic lesions of the femoropopliteal segment, **up to 180 mm**  
• Occlusion up to 150 mm |
| Balloon Sizes           | Diameter  
Length  
4-8 mm  
30-100 mm  
4-7 mm  
120-200 mm |
| Investigational Centers | 67 study centers: United States, Japan, New Zealand, Europe, Canada  
United States  
7 study centers: Belgium, Austria, New Zealand |
# Baseline Characteristics I Long Balloon Sub-study

## Demographics and Clinical History

<table>
<thead>
<tr>
<th>Demographics and Clinical History</th>
<th>Ranger DCB (N=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Year)</td>
<td>70.3±9.9</td>
</tr>
<tr>
<td>Female</td>
<td>26.9%</td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>98.1%</td>
</tr>
<tr>
<td>Black, or African heritage</td>
<td>1.9%</td>
</tr>
<tr>
<td>Smoking History</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>46.2%</td>
</tr>
<tr>
<td>Previous</td>
<td>44.2%</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>32.7%</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>82.4%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>71.2%</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease</td>
<td>18.0%</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>26.9%</td>
</tr>
<tr>
<td>History of Cerebrovascular Accident</td>
<td>3.8%</td>
</tr>
<tr>
<td>History of Renal Insufficiency</td>
<td>11.5%</td>
</tr>
</tbody>
</table>

## Lesion Characteristics (Core Lab)

<table>
<thead>
<tr>
<th>Lesion Characteristics</th>
<th>Ranger DCB (N=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion Length (mm)</td>
<td>130.8±47.2</td>
</tr>
<tr>
<td>Lesion Location</td>
<td></td>
</tr>
<tr>
<td>proximal SFA</td>
<td>30.8%</td>
</tr>
<tr>
<td>mid SFA</td>
<td>42.3%</td>
</tr>
<tr>
<td>distal SFA</td>
<td>26.9%</td>
</tr>
<tr>
<td>% Diameter Stenosis</td>
<td>84.2±15.1</td>
</tr>
<tr>
<td>Occlusion</td>
<td>38.5%</td>
</tr>
</tbody>
</table>

- Bare metal stent bail out 13.5% (7/52)

## Calcification (PACSS)

- Grade 0: 4%
- Grade 1: 15%
- Grade 2: 3.8%
- Grade 3: 34.6%
- Grade 4: 23.1%

## TASC II Type

- A: 38.5%
- B: 34.6%
- C: 23.1%
- D: 3.8%
Safety | Long Balloon Sub-study

- 12-Month MAE-free rate: 94.0% (47/50)
- All MAE were CD-TLR
- 12-month mortality 5.8% (3/52)

<table>
<thead>
<tr>
<th>Event</th>
<th>Ranger DCB (N=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-Month MAE</td>
<td>6.0% (3/50)</td>
</tr>
<tr>
<td>All-Cause Death at 1 Month</td>
<td>0.0% (0/50)</td>
</tr>
<tr>
<td>Target Limb Major Amputation</td>
<td>0.0% (0/50)</td>
</tr>
<tr>
<td>Target Lesion Revascularization</td>
<td>6.0% (3/50)</td>
</tr>
<tr>
<td>Clinically-Driven</td>
<td>6.0% (3/50)</td>
</tr>
</tbody>
</table>

MAEs were adjudicated by a Clinical Events Committee.
Effectiveness | Long Balloon Sub-study

Primary Patency

- **Long Ranger DCB**: 87.8%

Freedom from TLR

- **Long Ranger DCB**: 94.1%

Kaplan-Meier estimates with standard errors.
Primary patency KM estimate utilizing time-to-event of TLR up to 365 days and duplex ultrasound data at 12 months.
RANGER DCB Evidence Progression

Key Studies

**RANGER SFA (2016)**
- *N = 105*
- *Prospective RCT*
- *First-in-human demonstration of RANGER DCB efficacy and safety vs PTA*

**RANGER II SFA RCT (2019)**
- *N = 376*
- *Prospective RCT*
- *Pivotal demonstration of RANGER DCB efficacy and safety vs PTA in global patient sample*

**RANGER II SFA PK Substudy (2019)**
- *N = 12*
- *Pharmaco-kinetics substudy showed rapid systemic paclitaxel clearance (all patients < LoQ by 3 hours)*

**COMPARE* (2020)**
- *N = 414*
- *Prospective head-to-head RCT*
- *RANGER DCB (2µg/mm²) similar efficacy & safety vs high-dose IN.PACT DCB (3.5µg/mm²)*

**ELEGANCE Registry**
- *Up to 5000 patients*
- *Multicenter registry for RANGER DCB and Eluvia DES*
- *Real-world evidence*

---

3. Brodmann M, LINC 2020
4. Sachar R, VIVA 2019

DCB, drug-coated balloon; LoQ, limit of quantification; PK, pharmacokinetics; PTA, percutaneous transluminal angioplasty; RCT, randomized controlled trial

*This investigator-sponsored study is supported by grant funding from Boston Scientific. Boston Scientific is not responsible for the collection, analysis or reporting of the study which remains the sole responsibility of the investigators. Information for the use in countries with applicable product registrations.*
Conclusions

- RANGER II SFA results demonstrate consistent efficacy and safety results for patients treated with Ranger DCBs in standard or long lengths
- Low-dose Ranger DCB demonstrated superior effectiveness vs standard PTA through 1 year in the RANGER II SFA RCT
- Women and men showed similar primary patency and freedom from TLR benefit through 1 year following treatment with Ranger DCB in the RCT
- Safety and efficacy results from the Long Balloon Sub-study (balloon lengths up to 100 mm) are similar to the previously-reported results for the overall RANGER II SFA RCT

<table>
<thead>
<tr>
<th></th>
<th>RCT (N=376)</th>
<th>Women (n=136)</th>
<th>Long Balloons (N=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD-TLR</td>
<td>5.5% Ranger DCB vs 16.5% PTA (P=0.001)</td>
<td>6.3% Ranger DCB vs 25.0% PTA (P=0.0100)</td>
<td>6.0%</td>
</tr>
<tr>
<td>Primary Patency (KM)</td>
<td>89.8% Ranger DCB vs 79.0% PTA (log-rank P=0.0005)</td>
<td>88.2% Ranger DCB vs 68.4% PTA (log-rank P=0.0084)</td>
<td>87.8%</td>
</tr>
<tr>
<td>Lesion Length (mm)</td>
<td>82.5±48.9 (DCB arm)</td>
<td>75.8±53.2 (DCB arm)</td>
<td>130.8±47.2</td>
</tr>
</tbody>
</table>

1. Brodmann M, LINC 2020
2. Keirse K, LINC 2021
transluminal angioplasty. Studied. Patient has not been studied.

artery. Diameter of the vessel segment to be treated. The inflated length of the balloon (shoulder to shoulder)

Intended Use / Indications for Use

See Section 8.1 (in the eIFU) for further information.

Warnings

late mortality signal and the benefits and risks of available treatment options with their patients.

Carcinogenicity, Genotoxicity, and Reproductive Toxicology

No long-term studies in animals have been published in peer-reviewed literature to evaluate the
carcinogenic potential of paclitaxel. Paclitaxel interacts with microtubules; this is the major mechanism by
which it inhibits cell growth. One consequence is the loss of whole chromosomes via interactions with
spindle microtubules during cell division. As such, paclitaxel is defined as a clastogen (agent causing an
alteration in chromosome number). This indirect action is consistent with positive responses in in vitro and
in vivo micronucleus genotoxicity assays, which detect DNA fragments. Positive results have also been
reported for chromosomal aberrations in primary human lymphocytes. It is not known whether paclitaxel
has a separate direct action on DNA in the generation of DNA strand breaks or fragments. It is negative in
assays for gene mutation, including salmonella and CHO/HPRT. Paclitaxel administered via IV prior to
and during mating produced impairment of fertility in male and female rats at doses ≥ 1 mg/kg.

Administration of paclitaxel during the period of organogenesis to rabbits at doses of 3 mg/kg/day caused
embryo- and fetotoxicity. Maternal toxicity was also observed at this dose. No teratogenic effects were
observed at 1 mg/kg/day; teratogenic potential could not be assessed at higher doses due to excessive
fetal mortality. For comparison, the worst-case dose of paclitaxel delivered by the Ranger DCB (assuming
maximum size and number of balloons used in a lesion) is 9266 μg, which is approximately 6 and 19
times less than the dose that saw effects in rats and rabbits, respectively, when normalizing to body
weight.

Pre and Post Procedure Antiplatelet Therapy

It is strongly advised that the treating physician follow the Inter-Society Consensus (TASC II) Guidelines
recommendations (or other applicable country guidelines) for antiplatelet therapy pre- and postprocedure.
Brief Summary Cont.

Adverse Events

Potential adverse events include, but are not limited to, the following:

- Allergic reaction (device, contrast medium, medications)
- Arteriovenous fistula
- Death
- Hematoma
- Hemorrhage/Bleeding
- Hypotension/Hypertension
- Infection/Sepsis
- Pseudoaneurysm
- Thromboembolic episodes
- Vascular thrombosis
- Vessel injury (e.g., dissection, perforation, rupture)
- Vessel occlusion
- Vessel spasm

Potential adverse events not captured above that may be unique to the paclitaxel drug coating:

- Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or coating or its individual components
- Alopecia
- Anemia
- Blood product transfusion
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/Arthralgia
- Peripheral neuropathy

Apart from hypersensitivity reactions (allergic/immunologic reactions), the likelihood of paclitaxel related adverse events is low, due to the low exposure.

There may be other potential adverse events that are unforeseen at this time.