Discussion: SIRONA Trial Design
Head-to-Head Comparison of SIROlimus versus Paclitaxel Drug-Eluting BallooN Angioplasty in the Femoropopliteal Artery

Ulf Teichgräber, MD, MB
Disclosure

Speaker name:
Ulf Teichgräber, MD, MBA

I have the following potential conflicts of interest to report:

I am the leading principal investigator of the randomised-controlled SIRONA trial, a head-to-head comparison trial of sirolimus versus paclitaxel drug-eluting balloon angioplasty in the femoropopliteal artery.
Sirona at a glance

Randomized (1 : 1)

Safety and Efficacy of the Magic Touch PTA

478 patients

Patient blinded, Investigator unblinded

29 site in 2 countries

24 months recruitment

LINC 2021 – Sirolimus-coated balloons: what the FUTURE holds for PAD, Discussion: SIRONA, 26 Jan 2021, 09:55 – 10:00 a.m.
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# Trial Design and Endpoints

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Baseline</th>
<th>1 month</th>
<th>6 month</th>
<th>12 month</th>
<th>24 month</th>
<th>36 month</th>
<th>48 month</th>
<th>60 month</th>
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<tbody>
<tr>
<td><strong>Primary</strong></td>
<td>Patency Rate*</td>
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| **Secondary** | Composite of:  
- freedom from device and procedure-related death through 12 months  
- freedom from target limb major amputation and  
- clinically-driven TVR | WIQ | • TLR rate  
• Rutherford improvement  
• Walking capacity  
• EQ-5D-3L | | | | | |
| **Primary** | Composite of:  
- freedom from device and procedure-related death through 60 months  
- freedom from target limb major amputation and  
- clinically-driven TVR | | | | | | | Binary restenosis (via DUS) |

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**Study Endpoints**

<table>
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<tr>
<th><strong>Primary Endpoint</strong></th>
<th><strong>Secondary Endpoint</strong></th>
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<tbody>
<tr>
<td><strong>Efficacy:</strong> patency rate after one year defined as absence of clinically driven TLR (due to symptoms and drop of ABI of ≥ 20% or &gt; 0.15 when compared to post-procedure) or restenosis with PVR &gt; 2.4 evaluated by duplex ultrasound</td>
<td><strong>1. TLR rate</strong> at 6, 12, 24, 36, 48 and 60 months</td>
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<td><strong>Primary Safety:</strong> Composite of freedom from device and procedure-related death through 12 months post procedure as well as freedom from both target limb major amputation and clinically-driven target vessel revascularization</td>
<td><strong>2. Sustained clinical improvement:</strong> an improvement shift in the Rutherford classification of one class in amputation and TVR free surviving patients at 12 months</td>
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<td><strong>3. Walking capacity assessment:</strong></td>
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<td>a) Walking distance test measured by treadmill</td>
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<td></td>
<td>b) “Corridor” pain-free walking distance test</td>
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<td></td>
<td>c) Walking Impairment Questionnaire at 6, 12, 24, 36, 48 and 60 months.</td>
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<td><strong>4. Duplex-defined binary restenosis</strong> (PSVR &gt;2.4) of the target lesion post-procedure and at 6, 12 and 24 months or at any time of re-intervention</td>
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<td><strong>5. Quality of life assessment</strong> by EQ5D at 6, 12, 24, 36, 48 and 60 months</td>
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<td><strong>6. Secondary Safety:</strong> Composite of freedom from device and procedure-related, all cause death through 60 months post procedure as well as freedom from both target limb major amputation and clinically-driven target vessel revascularization.</td>
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### Key Eligibility Criteria

#### Inclusion
- Rutherford category 2-4
- De-novo stenotic / restenotic lesion with ≥ 70% stenosis
- Lesion length ≥ 2 cm and ≤ 20 cm
- Reference vessel diameter (RVD) ≥ 4 mm and ≤ 6.5 mm

#### Exclusion
- Severe calcified lesions (PTA resistant)
- Major amputation
- Previous surgery
- SFA or PPA disease in the opposite leg that requires treatment at the index procedure
Patient with PAD

Patient Consent Form

Baseline visit if all criteria are fulfilled

Eligible

Random allocation of patients into two treatment groups:
Ballon catheter with
1) Sirolimus
2) Paclitaxel

Angiography and final inclusion and exclusion criteria check, and pre-dilatation

Angioplasty (study intervention)

All these measures are taken in the angiography suite

After discharge, 7 follow-up visits over 5 years

Discharge

Study end

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Index procedure

Balloon length:
• Balloon sizing must match the reference vessel diameter distal to the target lesion and fully cover and extend slightly beyond the lesion length (about 1 cm of margin for both edges)
• Balloon inflation pressure should be at or beyond the nominal pressure, but the rated burst pressure (RBP) should never be exceeded

Inflation and pre-dilatation:
• Inflation time: min. 60 sec or longest time after SoC
• Dilatation time of **180 seconds** (3 minutes) is strongly recommended

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Follow-Up

**On-site**
- Physical examination with duplex of thigh concerned
- Queries about medication, health condition, walking test
- Walking capacity assessment

**Phone FU**
- Queries about medication, health condition, walking test

**Discharge**
- 1 Month

**Angioplasty**
- 6 Months
- 1 Year
- 2 Years
- 3 Years
- 4 Years
- 5 Years

**Study End**
DCB has been questioned after Katsanos et al. (2018) and Klumb et al. (2019) described an association between paclitaxel dose and mortality risk.

The authorities, such as BfArM, unanimously recommend further evaluation given the widespread use of paclitaxel in peripheral interventions in clinical practice.

SIRONA trial is currently the first trial worldwide that is ready to be initiated to collect additional evidence on patient level regarding this topic.

The safety alert initiated by the above-mentioned systematic reviews leads to the search of an alternative to PTX DCB.