Magic touch Sirolimus coated balloon: Coating technology and clinical trial programme

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Disclosure

Advisory Board /Consultant:

Abbott, Alvimedica, Bayer, Boston Scientific, Cook Medical, Cardionovum, CR Bard, Gardia Medical/Allium, Medtronic, Philips, Upstream Peripheral Technologies
Sirolimus inhibits mTOR and is part of the phophatidylinositol kinase-related family of serine/threonine kinases.

Paclitaxel binds to beta-tubulin and impairs microtubular disassembly and halts the cell cycle between G2 and M inhibits mTOR and is part of the phosphatidylinositol kinase-related family.
## PCB vs SCB Properties

<table>
<thead>
<tr>
<th>Factors</th>
<th>Paclitaxel Coated Balloon</th>
<th>Sirolimus Coated Balloon</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Nature</td>
<td>Highly Lipophilic</td>
<td>Less Lipophilic (potential disadvantage)</td>
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<tr>
<td>Drug Nature</td>
<td>Cytotoxic</td>
<td>Cytostatic</td>
</tr>
<tr>
<td>Drug Therapeutic Range</td>
<td>Narrow</td>
<td>Wide</td>
</tr>
<tr>
<td>Carrier</td>
<td>Urea, BHTC, Shellac</td>
<td>Phospholipid</td>
</tr>
<tr>
<td>Carrier Nature</td>
<td>Toxic</td>
<td>Biocompatible + Stabilizer</td>
</tr>
<tr>
<td>Coating complexity</td>
<td>Simple</td>
<td>Complex engineering</td>
</tr>
<tr>
<td>Coating Nature</td>
<td>Hydrophilic spacer</td>
<td>Encapsulation of drug</td>
</tr>
<tr>
<td>Mechanism of crossing the arterial wall</td>
<td>Van der Waals Forces</td>
<td>Fick's Law of Diffusion</td>
</tr>
<tr>
<td>Tissue Uptake</td>
<td>Partitioning of drug and drug binding slows transport leading accumulation of drug</td>
<td>Nanoparticles enable faster uptake through the lumen on vasa-vasorum and capillaries</td>
</tr>
</tbody>
</table>
Study Device (SCB)

• Drug delivery in 60 seconds
• Sub-micron particles for better adhesion
• Less drug loss
• Supersede limitations of Paclitaxel
• No permanent metallic cage
• No more toxic effects
• Nanotechnology advantage: easy penetration to deep layers of vessels

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Nanolute Technology

- Conversion of Sirolimus drug into sub-micron sized particles
- Encapsulation of sub-micron sized Sirolimus drug into highly biocompatible drug carrier – Phospholipid
- Phospholipid comprises of one hydrophilic head and two lipophilic tails, which improves adhesion property of encapsulated Sirolimus
- Upon inflation, drug carrier with Sirolimus drug inside gets transferred to the vessel wall following the principle of co-efficient diffusion
- Upon body PH variation, drug carrier mimics the body lipids and liberates Sirolimus
- The sub-micron sized Sirolimus drug particles penetrate the deeper layer of the vessel over a period

ADVANTAGES OF NANOLUTE TECHNOLOGY
- Facilitates better adhesion of Sirolimus on the balloon surface
- Effective drug transfer to the deepest layer of the vessel
- Better in-tissue Bioavailability of Sirolimus

LINC 2020 – Head-to-Head Comparison of SIROLimus versus Paclitaxel Drug-Eluting Balloon Angioplasty in the Femoropopliteal Artery
First in man study of clinical use and safety of Sirolimus coated PTA balloon in the treatment of infra-inguinal arterial disease

**XTOSI-STUDY**

Principal Investigator: Edward Choke  
Chief, Vascular and Endovascular Surgery, Sengkang General Hospital  
Associate Professor, DUKE-NUS Medical School, Singapore
Prospective, premarket, non-randomized, all comers single-arm trial

Target Enrollment: 50

- 6-month Freedom from Target Lesion Revascularisation: 88%
- **Safety endpoint:** No 30 day mortality and limb amputation AND no 6 month target lesion revascularisation: 84%
- **Efficacy endpoint:** 6-month Primary Patency: 80%

49 patients enrolled and 27 patients completed 6-months follow-up.
Primary patency according to lesion location

Above the knee

Efficacy endpoint:
SFA/Popliteal
6 month Primary Patency
83%

N=14

Below the knee

Efficacy endpoint:
Below the knee
6 month Primary Patency
77%

N=13
Multicentre, double blinded, randomised controlled trials (SFA and BTK) of sirolimus DCB versus standard PTA

**SIRONA SFA**

**BTK-RCT (PI Prof. Zeller)**
Study Design

- **Study Objective:** investigate the safety and efficacy of a sirolimus DCB in comparison to the most used DCBs in Germany in patients with symptomatic femoropopliteal artery disease

- **Study Design:** prospective, multi-center, 1:1 randomized

- Stratification according to lesion length into three groups
  - (≤ 10 cm / > 10 cm and ≤ 20 cm / > 20 cm and ≤ 30 cm)

- **Study Population:** 478 patients (239 per study arm) suffering peripheral artery disease ranging from intermittent claudication to critical limb ischemia
Planned Study Sites

Germany:
01 Jena
PD Dr. R. Aschenbach
University Hospital Jena

02 Leipzig
Prof. Dr. Dierk Scheinert
University Hospital Leipzig

03 Altenburg
Albrecht Bormann
Hospital Altenburger Land

04 Bad Krozingen
Prof. Dr. Thomas Zeller
University Heart Center Bad Krozingen

05 Bautzen
Dr. Uwe Kersten Wahl
Oberlausitz Clinic

06 Berlin
Dr. Ralf Langhoff
St. Gertrauden Clinic

07 Berlin
PD Dr. M. DeBocourt
Charité Hospital

08 Dresden
Prof. R.-T. Hoffmann
University Hospital Dresden

09 Karlsbad
Prof. Dr. E. Blessing
SRH-Clinic

10 Frankfurt
Dr. Christina Klöffling
Goethe University Hospital Frankfurt

11 Immenstadt
Dr. Wulf Ito
Cardiovascular Center Kempten

12 Magdeburg
Prof. Dr. Maciej Pech
University Hospital Magdeburg

13 Münster
Dr. Giovanni Torsello
St. Franziskus-Hospital

14 Münster
PD Dr. Nasser Malyar
University Hospital Münster

15 Radebeul
Dr. Torsten Fuss
Elbland Clinic

16 Riesa
Dr. Torsten Fuss
Elbland Clinic

17 Sonneberg
Dr. Markus Thieme
Medinos Clinic

18 Torgau
Dr. Lars Maiwald
Hospital Torgau

Austria:
19 Graz
Prof. M. Brodmann
University Hospital Graz

20 Wien
PD Dr. Martin Werner
Hanusch Hospital

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Study Endpoints

Primary Endpoint

Efficacy
• Patency rate

Safety
• Composite of:
  - freedom from all-cause death
  - freedom from target limb amputation
  - freedom from TVR through 12 months

Secondary Endpoint

Efficacy
• Freedom from TLR
• Rutherford improvement
• Walking capacity
• Binary restenosis (via DUS)
• EQ-5D-3L

Safety
• Composite of:
  - freedom from all-cause death
  - freedom from target limb amputation
  - freedom from TVR through 60 months
Key Eligibility Criteria

**Inclusion**

- Rutherford category 2-4
- **De-novo** stenotic / restenotic lesion with ≥ 70% stenosis
- Lesion length ≤ 30cm
- 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
Follow-Up

• followed up through 60 months to assess the incidence of restenosis by DUS and major adverse events (MAE)
• at 1, 6, 12, 24, 36, 48 and 60 months after index procedure

- on-site visits: at 6, 12 and 24 MF
- phone calls: at 1, 36, 48 and 60 MFU
## Trial Design and Endpoints

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<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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<tr>
<td><strong>Primary</strong></td>
<td>Patency Rate*</td>
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*defined as absence of clinically driven TLR (due to symptoms and drop of ABI of ≥ 20% or > 0.15 when compared to post-procedure) or restenosis with PVR > 2.4 evaluated by duplex ultrasound
Stratification

Randomization

1:1

478 subjects

239 subjects

≤ 10 cm/ > 10 cm
n=80

≤ 20 cm/ > 20 cm
n=80

≤ 30 cm
n=79

239 subjects

≤ 10 cm/ > 10 cm
n=80

≤ 20 cm/ > 20 cm
n=80

≤ 30 cm
n=79

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Be a part of the **SIRONA** study team!
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