Rationale & Design of SELUTION4BTK trial

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St. Antonius Hospital Nieuwegein, the Netherlands
Disclosure

Daniel van den Heuvel

I have the following potential conflicts of interest to report:

- [ ] Consulting
- [ ] Employment in industry
- [x] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [x] I do not have any potential conflict of interest
BTK Challenge for Intimal Drug Delivery: Barrier Tissue

Narula, et al. JACC 2018;72:2152-63
### Previous experience with Paclitaxel in BTK

**A Series of Negative Studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Endpoint Measure</th>
<th>DCB Group</th>
<th>PTA Group</th>
<th>Difference</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DCB</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In.PACT DEEP (JACC 2014;64_1568-76)</td>
<td>12-month Freedom from Restenosis</td>
<td>59.0%</td>
<td>64.5%</td>
<td>-5.5%</td>
<td>Further studies discontinued due to safety concerns</td>
</tr>
<tr>
<td></td>
<td>12-month Freedom from CD-TLR</td>
<td>88.1%</td>
<td>86.5%</td>
<td>1.6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12-month Freedom from Major Amp</td>
<td>91.2%</td>
<td>96.4%</td>
<td>-5.2%</td>
<td></td>
</tr>
<tr>
<td>BioLUX P-II (JACC Intv 2015;8:1614-22)</td>
<td>6-month Freedom from Restenosis</td>
<td>46.9%</td>
<td>58.6%</td>
<td>-11.7%</td>
<td>Negative efficacy result</td>
</tr>
<tr>
<td>SINGA-PACLI (Radiology 2021;300(3):715-724)</td>
<td>6-month superior Primary Patency</td>
<td>43%</td>
<td>38%</td>
<td>5%</td>
<td>Did not meet primary endpoints</td>
</tr>
<tr>
<td></td>
<td>12-month Freedom from Major Amp</td>
<td>59%</td>
<td>78%</td>
<td>-19%</td>
<td></td>
</tr>
<tr>
<td>Lutonix BTK (J Inv Card1:205-11iol 2019;3)</td>
<td>6-month Primary Efficacy Endpoint *</td>
<td>74.5%</td>
<td>63.5%</td>
<td>11.0%</td>
<td>Did not meet primary endpoint, signal dropout at 12 months</td>
</tr>
<tr>
<td></td>
<td>12-month Primary Efficacy Endpoint</td>
<td>60.4%</td>
<td>60.9%</td>
<td>-0.5%</td>
<td></td>
</tr>
<tr>
<td><strong>DES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAVAL (Presented by Hans van Overhagen at CIRSE 2022)</td>
<td>12-month Primary Patency</td>
<td>68.0%</td>
<td>76.0%</td>
<td>-8.0%</td>
<td>Did not meet primary effectiveness and safety endpoints</td>
</tr>
<tr>
<td></td>
<td>12-month Freedom from Major Adverse Event</td>
<td>91.6%</td>
<td>95.3%</td>
<td>-3.7%</td>
<td></td>
</tr>
</tbody>
</table>

* Composite of freedom from major amputation, target lesion occlusion, or CD-TLR

Adapted from G. Adams, VIVA 2020
Sirolimus Works Well in Short Stents in BTK

MicroReservoirs made from biodegradable polymer intermixed with molecular Sirolimus drug:

- Controlled and sustained drug release mechanism
- Maintains therapeutic effect in tissue over time (up to 90 days)

Proprietary Cell Adherent Technology – CAT™:

- CAT™ coating contains and protects MicroReservoirs during delivery allowing for a maximum transfer to vessel wall during inflation
- Enhanced drug retention allows for a lower drug dose concentration on the balloon surface (1 μg/mm²)
# SELUTION SLR - Clinical Trial Program
## Peripheral Program Enrolling Over 1900 Patients

### MEDALLIANCE Sponsored Trials

<table>
<thead>
<tr>
<th>Indication</th>
<th>Patient Numbers</th>
<th>Region</th>
<th>Design</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>SELUTION FIM</td>
<td>SFA/Popliteal</td>
<td>50</td>
<td>Germany</td>
<td>Single Arm</td>
</tr>
<tr>
<td>JAPAN SFA</td>
<td>SFA/Popliteal</td>
<td>134</td>
<td>Japan</td>
<td>Single Arm</td>
</tr>
<tr>
<td>CHINA SFA</td>
<td>SFA</td>
<td>139</td>
<td>China</td>
<td>RCT</td>
</tr>
<tr>
<td>SUCCESS PMS</td>
<td>SFA/BTK/Foot</td>
<td>772</td>
<td>Asia/Europe/LAM</td>
<td>Single Arm</td>
</tr>
<tr>
<td>SELUTION4BTK</td>
<td>BTK</td>
<td>377</td>
<td>Europe/US</td>
<td>RCT</td>
</tr>
<tr>
<td>SELUTION4SFA</td>
<td>SFA/Popliteal</td>
<td>300</td>
<td>Europe/US</td>
<td>RCT</td>
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### Physician-Initiated Trials

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<tr>
<td>PRESTIGE</td>
<td>BTK</td>
<td>25</td>
<td>Asia</td>
<td>24 Month Data</td>
</tr>
<tr>
<td>PRISTINE</td>
<td>BTK</td>
<td>75</td>
<td>Asia</td>
<td>12 Month Data</td>
</tr>
<tr>
<td>STEP</td>
<td>Foot</td>
<td>8</td>
<td>Austria</td>
<td>Completed</td>
</tr>
<tr>
<td>FLOW</td>
<td>SFA</td>
<td>70</td>
<td>Germany</td>
<td>1 Month Data</td>
</tr>
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</table>

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## PRESTIGE & PRISTINE – Patients with CLTI & BTK lesions

### Overview of the studies

<table>
<thead>
<tr>
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<th>Patients</th>
<th>Follow-up</th>
<th>Objectives</th>
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<tr>
<td><strong>PRESTIGE (N=25)</strong> - 24 mo FU available</td>
<td>25 patients from Asia</td>
<td>24 mo</td>
<td>➢ To evaluate the 6-months safety and performance outcome of the SELUTION SLR™ Sirolimus DCB on the treatment of long tibial occlusive lesions (TASC C and D) in patients with CLTI</td>
</tr>
<tr>
<td><strong>PRISTINE (N=75)</strong> - 12 mo FU available</td>
<td>75 patients from Asia</td>
<td>12 mo</td>
<td>➢ To evaluate the safety and performance outcome of the SELUTION™ Sirolimus-Coated SCB for the treatment of infra-inguinal occlusive lesions (TASC C and D) in CLTI</td>
</tr>
</tbody>
</table>

### Objectives

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<td>➢ Prospective, non-Randomized single-center trial, single arm</td>
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### Design

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<tr>
<td><strong>PRESTIGE</strong></td>
<td>25 patients from Asia</td>
<td>24 mo</td>
<td>➢ Treatment of 25 patients from Asia</td>
</tr>
<tr>
<td><strong>PRISTINE</strong></td>
<td>75 patients from Asia</td>
<td>12 mo</td>
<td>➢ Treatment of 75 patients from Asia</td>
</tr>
</tbody>
</table>

### Primary Endpoints

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<td><strong>PRESTIGE</strong></td>
<td>25 patients from Asia</td>
<td>24 mo</td>
<td>➢ Freedom from device- or procedure-related mortality through 30 days. ➢ Freedom from target lesion revascularization (TLR) at 6 months and 12 months</td>
</tr>
<tr>
<td><strong>PRISTINE</strong></td>
<td>75 patients from Asia</td>
<td>12 mo</td>
<td>➢ Freedom from device- and procedure-related mortality through 30 days. ➢ Freedom from clinically driven target lesion revascularization (TLR) within 6 months post-index procedure.</td>
</tr>
</tbody>
</table>

### Secondary Endpoints

<table>
<thead>
<tr>
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<th>Objectives</th>
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<tbody>
<tr>
<td><strong>PRESTIGE</strong></td>
<td>25 patients from Asia</td>
<td>24 mo</td>
<td>➢ Freedom from major target limb amputation ➢ Primary patency rate at 6 and 12M ➢ Technical success (ie, able to cross and dilate lesion to achieve &lt;30% residual stenosis) ➢ Clinical success (ie, improvement of Rutherford classification at follow-up) ➢ Wound healing (ie, complete closure of wound / &gt;70% healed)</td>
</tr>
<tr>
<td><strong>PRISTINE</strong></td>
<td>75 patients from Asia</td>
<td>12 mo</td>
<td>➢ Freedom from clinically-driven TLR at 6 and 12-month follow-up ➢ Freedom from major target limb amputation within 6- and 12-months post-index procedure ➢ Primary patency at 6- and 12-month follow-up ➢ Clinical success at follow-up</td>
</tr>
</tbody>
</table>

ClinicalTrials.gov ID: NCT04071782

ClinicalTrials.gov ID: NCT04534257

Tjun Yip Tang, Singapore General Hospital
Tze Tec Chong, Singapore General Hospital
PRESTIGE & PRISTINE – Patients with CLT & BTK lesions
Excellent sustained outcomes

**PRESTIGE** n=25, single operator
- TASC C&D
- 100% R5
- 64% at mod/sever calcification
- 56% moderate to high risk for amputation

**PRISTINE** n=75, multi operator
- TASC C&D
- More advanced wounds. 23% R6, 68% R5, 9% R4
- Higher calcification (88% mod/sever calcification)
- Higher risk of amputation (67% mod/high risk)

**Graphs**
- **Primary Patency**
  - 6 moFU: 81%, 12 mo FU: 93%
- **Freedom from TLR**
  - 6 moFU: 93%, 12 mo FU: 94%
- **AFS**
  - 6 moFU: 84%, 12 mo FU: 79%
- **Wound Healing**
  - 6 moFU: 82%, 12 mo FU: 79%
**SELUOTION4BTK IDE Trial – Currently Enrolling**

| **OBJECTIVES** | To demonstrate the superior efficacy and equivalent safety of the SELUTION SLR™ 014 DEB compared to plain (uncoated) balloon angioplasty in the treatment of peripheral arterial disease (PAD) in the BTK arteries in CLTI patients |
| **DESIGN** | • Prospective, multi-center, single blinded, RCT (1:1)  
• 377 patients (50% in USA)  
• 40 sites in USA, Europe, Singapore and Japan  
• FU up to 5 years |
| **PRIMARY ENDPOINTS** | • Efficacy: (Composite) Freedom from target lesion occlusion, above-ankle amputation, and clinically driven target lesion re-intervention (CD-TLR) at 6M  
• Safety: (Composite) Freedom from Major Adverse Limb Event (MALE) and all-cause perioperative death (POD) at 30 days |
| **FOLLOW-UP** | • 1-3-6 Months, 1,2,3,4,5 years |
| **STUDY STATUS** | • Enrolling |
| **PIs** | • US: Ehrin Armstrong  
• EU: Marianne Brodmann |

ClinicalTrials.gov ID: NCT05055297
SELUTION4BTK
Study Organization

**Steering Committee**
Principal Investigators:

- E. Armstrong (US)
- M. Brodmann (EU)

AND Kenny Rosenfield, Patrick Geraghty, Peter Gaines, Tjung Tang, Anahita Dua

- **Sponsor:**
  MedAlliance S.A.

- **CRO:** NAMSA, Hawthorne Effect

- **Independent Corelab:**
  - MedStar (Angio)
  - Vascore (DUPLEX)
  - Syntropic (Wound)

- **Independent Clinical Events Committee (CEC) & DSMB**
Enrolling sites*
*Current site list EU, Asia, NZ – Site selection process ongoing

**Singapore**
- Singapore General Hospital (T. Chong)
- Khoo Teck Puat Hospital (C. Leong)

**Hong Kong**
- Queen Mary Hospital (Y. Chan)
- The Chinese University of Hong Kong (B. Yan)

**Netherlands**
- St. Antonius Hospital (D. van den Heuvel)

**France**
- Hôpital Ambroise Paré (R. Coscas)
- Centre Hospitalier Universitaire (CHU) de Bordeaux (E. Ducasse)
- Hôpital St. Joseph (Y. Gouëffic)

**Switzerland**
- Opsedale Regionale di Lugano (J. Van den Berg)
- University of Bern (M. Schindewolf)

**Austria**
- LKH – Universitäts Klinikum Graz (M. Brodmann)

**Italy**
- San Raffaele Hospital (A. Kahlberg)
- Maria Cecilia Hospital (P. Sbarzaglia)
- Policlinico Abano - Abano Terme (M. Palena)
- Ospedale Policlinico San Martino Genoa (G. Pratesi)

**Germany**
- Klinikum Hochsauerland (M. Lichtenberg)
- University of Essen (C. Rammus)
- Universitäts-Herzzentrum Freiburg (T. Zeller)

**Greece**
- Patras University Hospital (K. Katsanos)

**New Zealand**
- Auckland City Hospital (A. Holden)

**Solution 4BTK**
FDA Study
## Key Inclusion Criteria

1. Patients with **Rutherford classification of 4-6**.
2. Patients with target lesion **distal to the tibial plateau and above the tibiotalar joint line** within the BTK arteries.
3. De novo or restenotic lesions
   - **RVD of ≥2.0 mm and ≤4.0 mm**
4. **Patent distal tibial and pedal run-off** to the foot
5. **Successful pre-dilatation** (defined by ≤ 30% residual stenosis, no distal embolization, and no Grade C or greater dissection)

## Key Exclusion Criteria

1. Patients with target vessel acute or subacute thrombosis
2. Planned Major Amputation
3. Required treatment via Pedal site
4. Any major surgical procedures performed 14 days before or planned 30 days after index procedure
5. Prior DCB, DES or BMS treatment of current target lesion(s).
6. Extensive tissue loss salvageable only with complex foot reconstruction
7. Acute Renal insufficiency (Chronic Renal Insufficiency allowed)
SELUTION4BTK – Treatment Flowchart

Pre-Randomization

Arterial Inflow Disease Present?

- **Successful Inflow Treatment**
  - **N**
  - Screening Failure
  - If inflow treated with SELUTION SLR™ 018 → 5-year FU

- **O**
  - BTK Target Lesion vessel prep
  - Successful vessel-preparation?
    - **N**
      - Screening Failure
      - If inflow treated with SELUTION SLR™ 018 → 5-year FU
    - **O**
      - Randomization 1:1

Study Treatment

- **SELUTION SLR™**
  - BTK Target Lesion treatment
    - SELUTION SLR™ 014
  - BTK Target Lesion treatment

- **POBA**
  - BTK Target Lesion treatment
  - POBA

Primary endpoints:

- Efficacy: (Composite) Freedom from target lesion occlusion, above-ankle amputation, and clinically driven target lesion re-intervention (CD-TLR) at 6M
- Safety: (Composite) Freedom from Major Adverse Limb Event (MALE) and all-cause perioperative death (POD) at 30 days
Take-home-message

- **SELUTION SLR** is a new generation drug eluting technology with:
  - **Sirolimus** as an anti-restenotic and anti-inflammatory drug with large therapeutic range
  - Sustained **drug release out to 90 days** to cover restenosis cascade
  - **Low drug dose of 1µg/mm²** due to improved drug transfer
  - **Smooth coating** surface for **improved delivery**
  - **Small & homogenous particulates** resulting in absence of slow flow phenomenon and reduced distal embolization

- **PRISTINE (n=75) & PRESTIGE (n=25)** have shown **early promising results** with SELUTION SLR in treatment of patients with CLI and below-the-knee lesions in complex real-world population

- **SELUTION4BTK RCT** is an IDE FDA trial which is currently enrolling globally & will evaluate the safety and efficacy of the **SELUTION SLR DEB compared to POBA** in treatment of patients with **BTK disease** in a randomized manner
Thank you!
Rationale & Design of SELUTION4BTK trial

Daniel van den Heuvel
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