SELUTION4BTK – a randomized clinical trial evaluating SELUTION SLR sirolimus-eluting balloon in the treatment of below-the-knee lesions in patients with chronic limb threatening ischemia

Marianne Brodmann
Medical University of Graz, Graz, Austria
Disclosure

Marianne Brodmann

I have the following potential conflicts of interest to report:

☑ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☐ 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</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</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>(JACC Intv 2015;8:1614-22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SINGA-PACLI</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>(Radiology 2021;300(3):715-724)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lutonix BTK</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>(J Inv Card1:205-11iol 2019;3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></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>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>(Presented by Hans van Overhagen at CIRSE 2022)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></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)
Proprietary MicroReservoir Technology
Sustained Sirolimus Release

- **MicroReservoirs ensure a controlled and sustained** Sirolimus drug release to maintain **therapeutic effect** in tissue over long period of time and up to 90 days.

**Arterial Tissue Drug Concentration**

<table>
<thead>
<tr>
<th>Drug Concentration [μg/g]</th>
<th>Med Alliance SELUTION - RAP</th>
<th>Bard LUTONIX - PAX</th>
<th>Medtronic IN.PACT - PAX</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>262</td>
<td>59</td>
<td>35</td>
</tr>
<tr>
<td>7 days</td>
<td>44</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>28 days</td>
<td>21</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>60 days</td>
<td>19</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**Drug Dose per Balloon Size**

- **Med Alliance SELUTION** - 1.0 μg/mm²
- **Bard LUTONIX** - 2.0 μg/mm²
- **Medtronic IN.PACT** - 3.5 μg/mm²

**En Face Scanning Electron Microscope at 24 hours**

Proprietary Balloon Coating Technology - CAT™
Drug Retention and Transfer

- Cell Adherent Technology – CAT™ coating provides an effective and improved Drug Transfer vs Competition allowing for lower drug dose of 1µg/mm²

<table>
<thead>
<tr>
<th></th>
<th>Med Alliance SELUTION</th>
<th>Bard LUTONIX</th>
<th>Medtronic IN.PACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost during procedure</td>
<td>36%</td>
<td>83%</td>
<td>83%</td>
</tr>
<tr>
<td>Retained on balloon</td>
<td>25%</td>
<td>12%</td>
<td>14%</td>
</tr>
<tr>
<td>Transferred to vessel (1 hr)</td>
<td>39%</td>
<td>5%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Proprietary Balloon Coating Technology - CAT™
Coating Integrity

Competitor A with crystalline coating (Paclitaxel)

SELUTION SLR™

NO FLAKING
Proprietary Balloon Coating Technology - CAT™
Deliverability

• Compared to sharp **Paclitaxel crystalline particles**, **SELUTION SLR™** offers a smoother balloon surface allowing for an excellent deliverability\(^1\)

\(^1\) SELUTION SLR™ Performance’s in term of Pushability and Crossability has been rated as “Very Good” by 73% of customers that have provided feedbacks with SELUTION SLR Evaluation Forms
Comparison with Crystalline Coatings
Small & Homogeneous Particulate Size

SELUTION SLR™ - MicroReservoirs Size vs. Available Paclitaxel Balloons

IN.PACT

LUTONIX

0.45µ Filter used in all tests

Images & Data on File @ MedAlliance
**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>SELUTION4SFA</td>
<td>SFA/Popliteal</td>
<td>300</td>
<td>Europe/US</td>
<td>RCT</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>
</tbody>
</table>

### Physician-Initiated 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>PRESTIGE</td>
<td>BTK</td>
<td>25</td>
<td>Asia</td>
<td>Single Arm</td>
</tr>
<tr>
<td>PRISTINE</td>
<td>BTK</td>
<td>75</td>
<td>Asia</td>
<td>Single Arm</td>
</tr>
<tr>
<td>STEP</td>
<td>Foot</td>
<td>8</td>
<td>Austria</td>
<td>Single Arm</td>
</tr>
<tr>
<td>FLOW</td>
<td>SFA</td>
<td>70</td>
<td>Germany</td>
<td>RCT</td>
</tr>
</tbody>
</table>
### PRESTIGE & PRISTINE

**Overview of the studies**

<table>
<thead>
<tr>
<th>PRESTIGE (N=25) - 24 mo FU available</th>
<th>PRISTINE (N=75) - 12 mo FU available</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OBJECTIVES</strong></td>
<td>➢ To evaluate the 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>DESIGN</strong></td>
<td>➢ Prospective, non-Randomized single-center trial, single arm</td>
</tr>
<tr>
<td></td>
<td>➢ Treatment of 25 patients from Asia</td>
</tr>
<tr>
<td><strong>PRIMARY ENDPOINTS</strong></td>
<td>➢ Freedom from device-or procedure-related mortality through 30 days</td>
</tr>
<tr>
<td></td>
<td>➢ Freedom from target lesion revascularization (TLR) at 6 months and 12 months</td>
</tr>
<tr>
<td><strong>SECONDARY ENDPOINTS</strong></td>
<td>➢ Freedom from major target limb amputation</td>
</tr>
<tr>
<td></td>
<td>➢ Primary patency rate at 6 and 12M</td>
</tr>
<tr>
<td></td>
<td>➢ Technical success (ie, able to cross and dilate lesion to achieve &lt;30% residual stenosis)</td>
</tr>
<tr>
<td></td>
<td>➢ Clinical success (ie, improvement of Rutherford classification at follow-up)</td>
</tr>
<tr>
<td></td>
<td>➢ Wound healing (ie, complete closure of wound / &gt;70% healed)</td>
</tr>
</tbody>
</table>

ClinicalTrials.gov ID: NCT04071782

| **OBJECTIVES** | ➢ 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 |
| **DESIGN** | ➢ Prospective, non-Randomized single-center trial, single arm |
| | ➢ Treatment of 75 patients from Asia |
| **PRIMARY ENDPOINTS** | ➢ Freedom from device- and procedure-related mortality through 30 days. |
| | ➢ Freedom from clinically driven target lesion revascularization (TLR) within 6 months post-index procedure. |
| **SECONDARY ENDPOINTS** | ➢ 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 |

ClinicalTrials.gov ID: NCT04534257

Tjun Yip Tang, Singapore General Hospital
Tze Tec Chong, Singapore General Hospital
### PRESTIGE: n=25, single operator

**Baseline**
- TASC C&D
- 100% R5
- 64% at mod/sever calcification
- 56% moderate to high risk for amputation

**Outcomes out to 6 months**
- Freedom from TLR: **92.6% (25/27)**
- Amputation-free survival (AFS): **84.0% (21/25)**
- Primary patency rate: **81.5% (22/27)**
- Wound healing: **81.8% (18/22)**

**Sustained Outcomes out to 18 months**
- Freedom TLR: **88.0% (22/25)**
- Amputation-free survival (AFS): **79.2% (19/24)**
- Wound healing: **78.9% (15/19)**

**Sustained Outcomes out to 24 months**
- Freedom TLR: **87.0% (20/23)**
- Amputation-free survival (AFS): **75% (18/24)**
- Wound healing: **94.4% (17/18)**

### PRISTINE: n=75, multi operator

**Baseline**
- 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**)

**Outcomes out to 6 months**
- Freedom from TLR: **84%**
- Amputation free survival: **84%**
- Primary Patency rate: **74%**
- Wound healing rate: **56%**

**Outcomes out to 12 months**
- Freedom from TLR: **74%**
- Amputation free survival: **72.6%**
- Wound healing: **79.2%**

**Outcomes out to 18 months**
- Freedom TLR: **88.0% (22/25)**
- Amputation-free survival (AFS): **79.2% (19/24)**
- Wound healing: **78.9% (15/19)**

**Outcomes out to 24 months**
- Freedom TLR: **87.0% (20/23)**
- Amputation-free survival (AFS): **75% (18/24)**
- Wound healing: **94.4% (17/18)**

---

Pls: Tjun Yip Tang and Tze Tec Chong, Singapore General Hospital

Tang, VIVA 2022

Chong, CX 2023

**PIs:** Tjun Yip Tang and Tze Tec Chong, Singapore General Hospital
SELUTION4BTK 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 – Treatment Flowchart

Pre-Randomization
All non-DCB/DES therapies (BMS, atherectomy, etc) allowable for inflow treatment. If DCB treatment required, SELUTION SLR™ 018 is to be used.

Arterial Inflow Disease Present?

Successful Inflow Treatment

BTK Target Lesion vessel prep

Successful vessel-preparation?

Randomization 1:1

If inflow treated with SELUTION SLR™ 018 → 5-year FU

Screening Failure

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

Study Treatment

SELUTION SLR™
BTK Target Lesion treatment

SELUTION SLR™ 014

POBA
BTK Target Lesion treatment

POBA

If inflow treated with SELUTION SLR™ 018 → 5-year FU
Enrolling sites*

*Current site list – 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 – Universitaets 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)

Greece
- Patras University Hospital (K. Katsanos)

New Zealand
- Auckland City Hospital (A. Holden)

Germany
- Klinikum Hochsauerland (M. Lichtenberg)
- University of Essen (C. Rammos)
- Universitäts-Herzzentrum Freiburg (T. Zeller)
North Carolina
- NC Heart & Vascular Research (G. Adams)
- Vascular Solutions of North Carolina (S. Rao)

Florida
- Palm Vascular Center (R. Beasley)
- Cardiac and Vascular Institute Research Foundation (A. Lee)
- Manatee Memorial Hospital (J. Mathews)

Arkansas
- Arkansas Heart Hospital (V. Lendel)
- St. Bernards Medical Center (B. Tedder)

California
- St. Helena Hospital (Y. Fai)
- Mission Cardiovascular Research Institute (A. Jain)

Ohio
- Cleveland Clinic (S. Steenberge)

Massachusetts
- Vascular Care Group (E. Arous)
- Beth Israel Medical Center (M. Wyers)
- University of Massachusetts Medical Center (D. Jones)

New York
- Columbia University (S. Parikh)

Rhode Island
- Miriam Hospital (P. Soukas)

Virginia
- Sentara Norfolk General Hospital (S. Steerman)

North Carolina
- NC Heart & Vascular Research (G. Adams)
- Vascular Solutions of North Carolina (S. Rao)

Florida
- Palm Vascular Center (R. Beasley)
- Cardiac and Vascular Institute Research Foundation (A. Lee)
- Manatee Memorial Hospital (J. Mathews)

Enrolling sites*
*Current site list – Site selection process ongoing
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!
SELUTION4BTK – a randomized clinical trial evaluating SELUTION SLR sirolimus-eluting balloon in the treatment of below-the-knee lesions in patients with chronic limb threatening ischemia

Marianne Brodmann
Medical University of Graz, Graz, Austria