Sirolimus and other – limus drug coatings will be the future

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@sahilparikhmd

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Columbia University Vagelos College of Physicians & Surgeons

Director, Endovascular Services
Center for Interventional Vascular Therapy
NewYork Presbyterian/Columbia University Irving Medical Center
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

<table>
<thead>
<tr>
<th>Affiliation/Financial Relationship</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institutional Research Support</td>
<td>Abbott Vascular, Veryan Medical, Acotec, Concept Medical, Shockwave Medical, TriReme Medical, Surmodics, Boston Scientific, MedAlliance</td>
</tr>
<tr>
<td>Advisory Board</td>
<td>Abbott, Medtronic, Boston Scientific, Cordis, Philips</td>
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<tr>
<td>Consulting</td>
<td>Terumo, Abiomed, Penumbra, Canon</td>
</tr>
<tr>
<td>Equity</td>
<td>Encompass Vascular, Adv NanoTherapies, eFemoral</td>
</tr>
</tbody>
</table>
No Mortality Signal was Identified Comparing Drugs

Network Meta-analysis: 38 trials, 18,023 pts

SES vs. BMS: HR 1.00 (0.82-1.25), p=0.89
PES vs. BMS: HR 1.03 (0.84-1.22), p=0.75
SES vs. PES: HR 0.96 (0.83-1.24), p=0.80

<table>
<thead>
<tr>
<th></th>
<th>Yr 1</th>
<th>Yr 2</th>
<th>Yr 3</th>
<th>Yr 4</th>
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<tbody>
<tr>
<td>BMS</td>
<td>4921</td>
<td>109/4904</td>
<td>48/3340</td>
<td>31/2264</td>
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<tr>
<td>PES</td>
<td>6331</td>
<td>138/6283</td>
<td>78/4263</td>
<td>32/2187</td>
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<tr>
<td>SES</td>
<td>6771</td>
<td>139/6730</td>
<td>72/4041</td>
<td>38/2340</td>
</tr>
</tbody>
</table>

Limus Agents Have Been Shown to be MORE EFFECTIVE in Coronary Artery Stenting

Network meta-analysis: 38 trials, 18,023 patients

Arterial Drug Uptake is a Function of Presentation Kinetics and Drug Properties

Parikh, et al. (Submitted)

Courtesy: S. Parikh, MD and E. Edelman, MD, PhD
Modes of Local Endovascular Drug Delivery

Target site

Endovascular modalities

- Drug Coated Stent
- Drug Eluting Stent
- Drug Eluting Balloon
- Drug “Coated” Balloon

Drug release

- FAST
- CONTROLLED/SUSTAINED
- FAST
- FAST

\[ \int_0^t [Drug] \approx \text{EFFECT} \]
Dosing Considerations
Balancing Safety and Efficacy

Arterial Paclitaxel Concentration
(ng/mg)

Time (Days)

Typical DCB Curve

Typical DES Curve

IMPROVE EFFICACY
(overlap restenotic cascade)

REDUCE COMPLICATIONS

TOXIC EFFECT

THERAPEUTIC WINDOW

NO EFFECT
Not all DCB Are Created Equal: Differential PK
So, if PTX is safe, what about Sirolimus? The bar is high

- Patency at 1 year > 80%
- Freedom from cd-TLR at 3-5y >70%
- ≤ MALE
- ≤ Mortality
TLR Rates of DES in the SFA are NOT the same as the Coronary Bed

Proprietary MicroReservoir Technology

• Creation of MicroReservoirs combining sirolimus & biodegradable polymer
  • Sirolimus - a proven safe & effective cytostatic drug
  • Offering a wider therapeutic range

MicroReservoirs: Miniature Drug-Delivery

• Optimal size MicroReservoirs to achieve pharmacokinetic release profile comparable to best in class DES
  • Consistent and predictable drug release
  • Sustained therapeutic effect for up to 90 days¹

Cell Adherent Technology (CAT™)

Proprietary amphipathic lipid technology which binds MicroReservoirs to the balloon surface

• Contains and protects micro-reservoirs during insertion and inflation
• Enhances drug retention and bioavailability, allowing for a lower drug dose concentration on the balloon surface (1 μg/mm²)
  • Optimizes transfer of MicroReservoirs to the tissue and maximizes the cellular uptake of sirolimus

¹Drug concentration evident in MicroReservoirs and tissue - Data on file at M.A. Med Alliance SA
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**
Sirolimus (RAP) versus Paclitaxel (PAX)

- **Med Alliance SELUTION - RAP**
- **Bard LUTONIX - PAX**
- **Medtronic IN.PACT - PAX**

<table>
<thead>
<tr>
<th>Time</th>
<th>Sirolimus (ug/g)</th>
<th>Paclitaxel (ug/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 hour</td>
<td>262</td>
<td>59</td>
</tr>
<tr>
<td>7 days</td>
<td>44</td>
<td>35</td>
</tr>
<tr>
<td>28 days</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>60 days</td>
<td>19</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**

<table>
<thead>
<tr>
<th>Balloon Size</th>
<th>Drug Dose [mg]</th>
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<tbody>
<tr>
<td>4.0x40</td>
<td>0.5</td>
</tr>
<tr>
<td>6.0x150</td>
<td>2.8</td>
</tr>
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</table>

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

---

<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>
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</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>
12-month results from SELUTION SFA Japan trial

Safety and efficacy of a novel sirolimus-coated balloon for the treatment of femoropopliteal lesions in Japanese population

Osamu Iida¹, Yoshimitsu Soga²

¹) Osaka Police Hospital, Cardiovascular Center
²) Kokura Memorial Hospital, Department of Cardiology
# SELUTION SFA Japan (MDK-1901) Study Design

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>OBJECTIVES</strong></td>
<td>To assess the safety and efficacy of the SELUTION SLR DEB in treatment of in the treatment of stenosis or occlusion of SFA and/or PA in patients with Rutherford category 2-4</td>
</tr>
<tr>
<td><strong>DESIGN</strong></td>
<td>Prospective, controlled, multi-center, open, single-arm clinical investigation</td>
</tr>
<tr>
<td></td>
<td>134 subjects in 13 sites in Japan</td>
</tr>
<tr>
<td><strong>PRIMARY ENDPOINT</strong></td>
<td>Primary Endpoint: primary patency of the target lesion – 12M</td>
</tr>
<tr>
<td></td>
<td>Primary patency defined as freedom from clinically driven TLR and freedom from restenosis as determined by DUS (PSVR≥2.5)</td>
</tr>
<tr>
<td><strong>FOLLOW-UP</strong></td>
<td>30 days, 6, 12, 24 and 36 months post-procedure</td>
</tr>
<tr>
<td><strong>PIs</strong></td>
<td>Osamu Iida</td>
</tr>
<tr>
<td></td>
<td>Yoshimitsu Soga</td>
</tr>
</tbody>
</table>
SELUTION SFA Japan

SELUTION SFA JAPAN - Efficacy outcomes

Primary Endpoint – 12M Primary Patency

- Days post Index Procedure
- Primary Patency: freedom from clinically driven TLR and freedom from restenosis as determined by DUSS (PSVR ≥ 2.5)
- Numbers at risk: 134
- Days: 0, 180, 365
- Patency rate: 87.9%

Secondary Endpoint – 12M freedom from TLR

- Days post Index Procedure
- Numbers at risk: 134
- Days: 0, 180, 365
- Freedom from TLR rate: 97.0%

O. Iida, LINX 2023
**SUCCESS PTA Study**

**SelUtion, safety, effiCaCy, hEalth economicS & promS**

Interim analysis:
Patients enrolled between Feb 2020 and Jul 2022

| OBJECTIVES | • Global post-market surveillance study of the SELUTION SLR DEB  
• Collect real world safety, efficacy, health economics and Patient Reported Outcome Measure (PROM) data on the use of the SELUTION SLR DEB |
| --- | --- |
| DESIGN | • Single study covering all peripheral indications (SFA, BTK, Foot)  
• 722 patients in 50 sites around Europe, Asia, South America |
| PRIMARY ENDPOINTS | • Clinically Driven Target Lesion Revascularization (CD-TLR) at 12M |
| SECONDARY ENDPOINTS | • Device success & Procedure success (primary and secondary)  
• Major Adverse Limb Events (MALE) composite endpoint  
• Death  
• TLR & TVR - including time to first CD-TLR  
• Target limb revascularization, thrombosis at the target site and amputation  
• Change in Rutherford score and ABI from baseline  
• Wound status  
• Kawarada classification (Only patients with foot symptoms) |
| FOLLOW-UP | • Clinical Follow-up: 6 months, 1 year  
• Telephone Follow-up: 2, 3, 4, 5 years |
| PRINCIPAL INVESTIGATOR | • Michael Lichtenberg, Arnsberg, Germany |

ClinicalTrials.gov ID: NCT04776434
SUCCESS PTA Post Market Real-World Study – Interim Analysis (n=321 pts)
Clinical Outcomes up to 6 Months (180 Days)

<table>
<thead>
<tr>
<th>Clinical outcome (event rates)</th>
<th>Up to 1 month (*N = 319)</th>
<th>Up to 6 months (*N=302)</th>
</tr>
</thead>
<tbody>
<tr>
<td>* patients with available vital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All death</td>
<td>1 (0.3%)</td>
<td>7 (2.3%)</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>0 (0%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Clinical outcome (event rates)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>γ patients with compliant FU at 6M</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Up to 1 month (* N = 315 )</td>
<td>Up to 6 months (* N = 282 )</td>
<td></td>
</tr>
<tr>
<td>Target limb amputation</td>
<td>4 (1.3%)</td>
<td>4 (1.4%)</td>
</tr>
<tr>
<td>Major amputation</td>
<td>1 (0.3%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Minor amputation</td>
<td>3 (0.9%)</td>
<td>3 (1.1%)</td>
</tr>
<tr>
<td>Clinical-driven Target limb revascularization</td>
<td>2 (0.6%)</td>
<td>14 (5%)</td>
</tr>
<tr>
<td>Clinically-driven target-lesion revascularization (CD-TLR)</td>
<td>1 (0.3%)</td>
<td>10 (3.5%)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Major Cardiac Events (MI, Stroke, Cardiovascular death) (MI, Stroke, Cardiovascular death)</td>
<td>0 (0%)</td>
<td>3 (1.06%)</td>
</tr>
<tr>
<td>Major Adverse Limb Events (MALE)</td>
<td>Severe index limb ischemia leading to an intervention or major vascular amputation (above the ankle)</td>
<td>5 (1.6%)</td>
</tr>
</tbody>
</table>
### OBJECTIVES
➢ To demonstrate the safety and efficacy of the SELUTION SLR™ 018 DEB compared to plain (uncoated) balloon angioplasty in the treatment of PAD in the SFA and PPA artery.

### DESIGN
➢ Prospective, multi-center, single blinded, randomized, controlled, superiority clinical trial
➢ 300 subjects will be enrolled at approximately 40 sites across the US, Europe, Canada and Asia.

### PRIMARY ENDPOINTS
➢ Freedom from death (device and procedure related) – **30 Days**
➢ Primary patency of the target lesion – **12M**

### FOLLOW-UP
➢ Subjects will be followed for 5 years post-procedure

### PIs
➢ Thomas Zeller
➢ S Jay Mathews

ClinicalTrials.gov ID: NCT05132361
MagicTouch PTA
Sirolimus Coated Balloon

Designed by NANOLUTE TECHNOLOGY
DEPICTION OF **NANOLUTE TECHNOLOGY**

- Sirolimus sub-micron particle
- Phospholipid drug carrier sub-micron particle
- Sirolimus encapsulated in phospholipid drug carrier
- Dedicated spray coating on balloon surface
MagicTouch PK Data (Porcine Iliofemoral GLP)

Sirolimus Blood Levels

Sirolimus ng/ml

Sirolimus ng/g

Treated Segment Iliofemoral

Courtesy: Aloke Finn, MD
CLINICAL STUDIES - PTA

X-TOSI

PI: Prof. Edward Choke
Sponsored, Observational, Prospective, All-comers, Single Arm, Real-world To evaluate the efficacy and safety of Magic Touch in the treatment of infrainguinal peripheral arterial disease

50 Patients
Enrollment closed

BEYOND X-TOSI

PI: Prof. Edward Choke
Investigator-Initiated, Real world data for complex CLTI patients treated with MagicTouch PTA sirolimus coated balloon

216 Patients
Real World data
X-TOSI

Clinical efficacy and safety of the Magic Touch PTA Sirolimus coated balloon for SFA and BTK lesions
## Primary endpoint: 6 month Primary Patency

### 6 month outcomes

<table>
<thead>
<tr>
<th></th>
<th>All (N=50)</th>
<th>Femoropopliteal (N=20)</th>
<th>Below the knee (N=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary patency</td>
<td>80.0%</td>
<td>88.2%</td>
<td>74.0%</td>
</tr>
</tbody>
</table>

For comparison:
- RANGER RCT 87.0%
- LEVANT 2 LUTONIX 90.0%
- SINGAPACLI 42.0%

---

**Figure 2.** Primary patency.

- Number at risk (number censored)
  - Femoropopliteal: 29 (2) 15 (3) 11 (6)
  - Below the knee: 29 (2) 17 (1) 13 (8)
DEBATE BTK DUeIL
PI: Dr. Francesco Liistro
Investigator-initiated, Randomised, Single Blind, Multicentre trial, to compare the remote patency of the sirolimus (Magic Touch) vs. paclitaxel (Lithos) release balloon, in patients undergoing tibial artery revascularization.

FUTURE SFA- ASIA
PI: Prof. Edward Choke
Sponsored, Randomised, Double blind, Multicentres (130 SCB : 65 PTA) To determine the effectiveness (primary patency) of Magic Touch versus standard percutaneous transluminal angioplasty for the treatment of below the knee arterial disease

FUTURE BTK- ASIA
PI: Prof. Edward Choke
Sponsored, Randomised, Double blind, Multicentres (130 SCB : 65 PTA) To determine the effectiveness (primary patency) of Magic Touch versus standard percutaneous transluminal angioplasty for the treatment of below the knee arterial disease

172 Patients
76 Patients Enrolled

279 Patients
56 Patients Enrolled

219 Patients
78 Patients Enrolled
Design:
Prospective registry of all lower limb angioplasty procedures

Single centre: Sengkang General Hospital, Singapore

Sirolimus coated balloon versus Standard balloon

Included if
1. CLTI patients Rutherford 4 to 6
2. De novo lesions

Excluded if
1. Received paclitaxel device, thrombolysis or atherectomy device

Sirolimus coated balloon
(n=141)

Standard balloon
(n=213)
HOPE Registry
Ethical Board approval CIRB Ref: 2019/2637

Between August 2018 and Oct 2021

Clinical Outcomes
Clinically Driven Target Lesion Revascularisation (TLR)
Amputation
Amputation Free Survival (AFS)
Overall survival

Sirolimus coated balloon
(n=141)

Standard balloon
(n=213)
Sirolimus coated balloon associated with **38% reduction in TLR (p=0.039)**

**Graph:**
- **Freedom from TLR**
- **12 month**
- **Sirolimus CB:** 80.3%
- **Standard uncoated balloon:** 70.6%
- **HR 0.62**
  - **(95% CI 0.39-0.98)**
  - **p=0.039**

Adjusted for comorbidities (age, sex, race, stroke history, IHD, COPD, I ESRF, hypertension, smoking, ASA score, preoperative antiplatelet/anticoagulation, WIFI score) and lesion (lesion length, retrograde access, severity of calcification, use of BTK bailout stent)
Sirolimus coated balloon tended towards lower rates of major limb amputation (p=0.068).

**Adjusted for comorbidities (age, sex, race, stroke history, IHD, COPD, I ESRF, hypertension, smoking, ASA score, preoperative antiplatelet/anticoagulation, WIFI score) and lesion (lesion length, retrograde access, severity of calcification, use of BTK bailout stent)**
Sirolimus coated balloon associated with higher AFS (p=0.019)

Amputation Free Survival

Adjusted for comorbidities (age, sex, race, stroke history, IHD, COPD, I ESRF, hypertension, smoking, ASA score, preoperative antiplatelet/anticoagulation, WIFI score) and lesion (lesion length, retrograde access, severity of calcification, use of BTK bailout stent)
Sirolimus coated balloon has similar Overall Survival

Adjusted for comorbidities (age, sex, race, stroke history, IHD, COPD, I ESRF, hypertension, smoking, ASA score, preoperative antiplatelet/anticoagulation, WIFI score) and lesion (lesion length, retrograde access, severity of calcification, use of BTK bailout stent)
**SIRONA - Germany**

PI: Dott. Ulf Teichgräber

Investigator-initiated, Randomised, Open Label, Multicentre trial, to investigate the safety and efficacy of Magic Touch in comparison to the most used DCBs in Germany in patients with symptomatic femoropopliteal artery disease

Enrollment Completed

Patients

478

830 Patients Enrolled

---

**SirPAD - Zurich**

PI: Prof. Nil Kucher

Investigator-initiated, Randomised, multicenter trial, to evaluate that Magic Touch is non-inferior to POBA in infra-inguinal angioplasty to prevent one-year major adverse limb events in a representative population (‘all-comers’) of patients with PAD

830 Patients Enrolled

Patients

1132
Investigator-initiated, Randomised, Open Label, Multicentre trial, to evaluate the effectiveness of the MagicTouch compared to POBA for the treatment of native artery infrapopliteal occlusions in patients presenting with severe claudication or critical limb ischemia (Rutherford 3-6).

LIMES - Germany
PI: Dott. Ulf Teichgräber
250 Patients
67 Patients Enrolled

MATSA - Spain
PI: Dra. Claudia Riera; Co-PI: Dr. Marc Sirvent
150 Patients
20 Patients Enrolled
UPCOMING CLINICAL TRIALS - PTA

MAGICAL BTK - IDE FDA

PIs: Drs. Sahil Parikh, Brian Derubertis, Eric Secemsky

Sponsored, Prospective, Randomized (2 Magic Touch :1 PTA), multicenter study determine the effectiveness (primary patency) and safety of the sirolimus drug coated balloon (DCB) versus standard percutaneous transluminal angioplasty (PTA) for the treatment of below the knee arterial disease.

360 Patients

Q3 2023

MAGICAL SFA - IDE FDA

PI: Drs. Sahil Parikh, Brian Derubertis, Eric Secemsky

Sponsored, Prospective, randomized, multi-center study to compare the Magic Touch PTA Sirolimus Coated Balloon with Paclitaxel-coated DCB for treatment of high grade stenotic or occluded lesions in SFA and / or P1 segment of the popliteal artery (PA) in PAD patients.

478 Patients

Q3 2023
LIFE-BTK Randomized Multicenter Trial

PIVOTAL INVESTIGATION OF SAFETY AND EFFICACY OF DRS FOR BTK TREATMENT

Prospective, randomized, multicenter, US and OUS single-blind trial
261 patients randomized
2:1 Esprit™ BTK vs. PTA

5-YEAR FOLLOW-UP

www.life-btk.com

TRIAL LEADERSHIP
Ramon Varcoe MBBS, MS, FRACS, PhD; Sahil Parikh MD, FACC, FSCAI; Brian DeRubertis MD, FACS

Safety Endpoint @ 6 months: MALE+POD

Efficacy Endpoint @ 12 months: Primary Patency + Limb Salvage
LIFE-BTK Randomized Multicenter Trial

Study Population

Critical Limb Ischemia RB 4-5

Proximal 2/3 of native infrapopliteal arteries

RVD ≥ 2.5 mm and ≤ 4.0 mm

Maximum 2 de novo/restenotic (from prior PTA) infrapopliteal lesions, each with ≥70% stenosis

Total scaffold length to cover target lesion must be ≤ 170 mm. Total scaffold length among all target lesions must be ≤ 170 mm
Bioresorbable Vascular Scaffolds: LIFE-BTK Trial

- Total activated and enrolling sites: 52
- Total randomized patients: 261

Data as of September 14, 2022
## Bioresorbable Polymers for BRS

**Tyrocore is the First Polymer Invented for BRS**

Tyrocore Invented in Collaboration between REVA Medical & Rutgers University

<table>
<thead>
<tr>
<th>2nd and 3rd Generation Tyrocore BRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fantom</td>
</tr>
<tr>
<td>Fantom Encore &amp; MOTIV BTK</td>
</tr>
</tbody>
</table>

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**All Other Players Use Off-the-Shelf Materials**

<table>
<thead>
<tr>
<th>PLLA Used in Surgical Products</th>
<th>1st Generation PLLA BRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone Screws Orthopedic Surgery</td>
<td>Absorb</td>
</tr>
<tr>
<td>Thread Plastic Surgery</td>
<td>DESolve</td>
</tr>
</tbody>
</table>

---

Courtesy Ehrin Armstrong, MD
# MOTIV Bioresorbable Scaffold  
## Device Specifications Overview

<table>
<thead>
<tr>
<th>Description</th>
<th>Bioresorbable BTK scaffold</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Scaffold material</strong></td>
<td>Tyrocore™</td>
</tr>
<tr>
<td><strong>Coating material</strong></td>
<td>Tyrocore</td>
</tr>
<tr>
<td><strong>Drug</strong></td>
<td>Sirolimus</td>
</tr>
<tr>
<td><strong>Drug dose</strong></td>
<td>1.97 µg/mm</td>
</tr>
<tr>
<td><strong>Shortening</strong></td>
<td>1% (lengthening)</td>
</tr>
<tr>
<td><strong>Maximum expansion diameter</strong></td>
<td></td>
</tr>
<tr>
<td>Size (mm)</td>
<td>Max Expansion (mm)</td>
</tr>
<tr>
<td>2.5</td>
<td>3.25</td>
</tr>
<tr>
<td>3.0</td>
<td>3.75</td>
</tr>
<tr>
<td>3.5</td>
<td>4.0</td>
</tr>
<tr>
<td>4.0</td>
<td>4.5</td>
</tr>
<tr>
<td><strong>Catheter type</strong></td>
<td>Rapid exchange</td>
</tr>
<tr>
<td><strong>Guide catheter compatibility</strong></td>
<td>6F</td>
</tr>
<tr>
<td><strong>Working catheter length</strong></td>
<td>139 cm</td>
</tr>
<tr>
<td><strong>Scaffold lengths</strong></td>
<td>Current</td>
</tr>
<tr>
<td></td>
<td>12, 18, 24 mm</td>
</tr>
<tr>
<td></td>
<td>36, 48, 60 mm</td>
</tr>
<tr>
<td><strong>Nominal pressure</strong></td>
<td>7 atm</td>
</tr>
<tr>
<td><strong>Rated burst pressure</strong></td>
<td>18 atm</td>
</tr>
<tr>
<td><strong>Balloon material</strong></td>
<td>Nylon</td>
</tr>
</tbody>
</table>
MOTIV™ Bioresorbable Scaffold
Preliminary Study Outcomes

- 99% Technical Success in all patients (71/72 Scaffolds)
- Primary Patency
  - 6-month final result: 90% Patency (N=47 patients/48 limbs)\(^1\)
- Clinically Driven TLR rate: 3% (two events across all study patients)
- Limb Salvage Rate: 97% (across all study patients)
  - One patient had a lower leg amputation at ~1-month due to wound healing disorder; reported as unrelated to the MOTIV scaffold
  - One patient had an amputation of study limb at ~4 months due to a septic wound infection; reported as unrelated to the MOTIV scaffold
- **8 deaths (14% of patients)**
  - All deaths outside of 30d and not device or procedure related
  - Heart & Respiratory Failure = 1, Septic Shock/Renal Failure = 4, Multi-Organ Failure = 3

---

\(^1\) PsVR data for 48 patients: 12 patients completed 6 month visit; no device related adverse events; PsVR not recorded

\(^2\) 79 patients have completed the 12 month follow-up of HMPR/0079

Courtesy: Thomas Rand, CIRSE 2022
The R3 Vascular Drug-Eluting Biodegradable Scaffold in Below the Knee Vessels: Interim Results from the RESOLV-I Trial

Prof. Marianne Brodmann, MD
Division of Angiology, Medical University of Graz, Austria
## MAGNITUDE® Sirolimus-Eluting BRS

<table>
<thead>
<tr>
<th>Design Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymer</td>
<td>Ultra High MW-Poly-L-Lactide (PLLA)</td>
</tr>
<tr>
<td>Diameters</td>
<td>3.0 and 3.5 mm</td>
</tr>
<tr>
<td>Lengths</td>
<td>18 and 38 mm</td>
</tr>
<tr>
<td>Wall Thickness</td>
<td>98 µm All Scaffold Sizes</td>
</tr>
<tr>
<td>Surface Coverage Area (at RBP)</td>
<td>22 – 27%*</td>
</tr>
<tr>
<td>Drug Coating</td>
<td>1:1 Poly D L-lactide:Sirolimus</td>
</tr>
<tr>
<td>Drug Content</td>
<td>144 – 291 µg*</td>
</tr>
<tr>
<td>Drug Density</td>
<td>96 µg/cm²</td>
</tr>
<tr>
<td>Inflation Pressures</td>
<td>Nominal: 7 to 9 ATM*</td>
</tr>
<tr>
<td></td>
<td>RBP: 16 ATM</td>
</tr>
<tr>
<td>Guide Catheter Size</td>
<td>6 French Compatible</td>
</tr>
</tbody>
</table>

*Depending on scaffold size
# 6-Month Angiographic Core Lab Analysis

<table>
<thead>
<tr>
<th>QCA Measurements</th>
<th>Baseline Procedure (n = 21 Lesions)</th>
<th>Post-BRS Implantation (n = 21 Lesions)</th>
<th>6-Month Follow-Up (n = 9 Lesions)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean ± SD or % (Range)</strong></td>
<td>Interpolated RVD (mm)</td>
<td>3.20 ± 0.36 (2.47 – 3.87)</td>
<td>3.45 ± 0.31 (2.90 – 4.05)</td>
</tr>
<tr>
<td></td>
<td>MLD (mm)</td>
<td>0.68 ± 0.37 (0 – 1.35)</td>
<td>2.95 ± 0.32 (2.25 – 3.45)</td>
</tr>
<tr>
<td></td>
<td>Late Lumen Loss (mm)</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>Diameter Stenosis (%)</td>
<td>78.74 ± 10.83 (62.71 – 100)</td>
<td>14.31 ± 6.89 (3.90 – 27.88)</td>
</tr>
<tr>
<td></td>
<td>Binary Restenosis (% , n)</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td><strong>In-Scaffold Analysis</strong></td>
<td>MLD (mm)</td>
<td>---</td>
<td>3.07 ± 0.39 (2.25 – 3.64)</td>
</tr>
<tr>
<td></td>
<td>Late Lumen Loss (mm)</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>Diameter Stenosis (%)</td>
<td>---</td>
<td>11.39 ± 7.51 (-0.83 – 27.88)</td>
</tr>
</tbody>
</table>
Drug elution from stent struts

The problem: Drugs on DES (e.g. Sirolimus) have short diffusion distances
- Creates non-uniform drug distribution in vessel wall
- Requires high doses of drug that delay healing
- Sub-therapeutic drug levels in large arteries (e.g. SFA)
Hybrid Stent Components

Metal (NiTinol) radial structure for vessel support
- High radial strength
- Self-expanding spiral design

Polymeric mesh covering for longitudinal stability
- Infinite flexibility and fatigue resistance
- Preservation of side branches and vessel compatibility
Drug elution from stent envelope

- The solution: Drug elution from fibrous mesh covering entire stent envelope
  - Short diffusion distance allows uniform drug distribution
  - Lower overall drug load
  - Therapeutic levels in every vessel size

Mesh-covered DES

Uniform drug concentration

Polymer fibers

Drug
Area vs Point Elution

Regular DES

ChampioNIR DES

Spatially uniform dosing w/o regional gradients
Clinical application

**Coronary (IoNIR stent)**
Improved local healing due to lower toxicity
4X reduction in total drug dose

<table>
<thead>
<tr>
<th>Total drug on 4.0X16mm stent [µg]</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>EluNIR</td>
<td>115*</td>
</tr>
<tr>
<td>Synergy</td>
<td>125</td>
</tr>
<tr>
<td>Xience</td>
<td>98**</td>
</tr>
<tr>
<td>Xience</td>
<td>98**</td>
</tr>
<tr>
<td>Onyx</td>
<td>132**</td>
</tr>
<tr>
<td>Orsiro</td>
<td>113**</td>
</tr>
<tr>
<td>IoNIR</td>
<td>31</td>
</tr>
</tbody>
</table>

FIM study (IonMAN) underway

* 17mm
** 15mm

**Peripheral (ChampioNIR SFA stent)**
Therapeutic dosing with **Sirolimus** over time

Drug in Tissue – Swine SFA Implantation

Therapeutic window for ‘limus’ drug
Where are we with the data on Limus?

Summary

- Sirolimus and its analogues have demonstrated superior efficacy in Coronary intervention.
- Due to differential binding and PK/PD in peripheral arteries, we’ve yet been unable to match these results in the SFA or BTK.
- New formulations of sirolimus eluting devices have been developed for peripheral applications and are now ACTIVELY being studied against a variety of comparators – they likely represent a significant wave of innovation in local vascular drug delivery.
Sirolimus and other – limus drug coatings will be the future

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