Do we have enough evidence for limus devices to replace PTX?

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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><strong>Institutional Research Support</strong></td>
<td>• Abbott Vascular, Veryan Medical, Acotec, Concept Medical, Shockwave Medical, TriReme Medical, Surmodics, Boston Scientific, MedAlliance</td>
</tr>
<tr>
<td><strong>Advisory Board</strong></td>
<td>• Abbott, Medtronic, Boston Scientific, Cordis, Philips</td>
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<td><strong>Consulting</strong></td>
<td>• Terumo, Abiomed, Penumbra, Canon</td>
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<tr>
<td><strong>Equity</strong></td>
<td>• Encompass Vascular, Adv NanoTherapies, eFemoral</td>
</tr>
</tbody>
</table>
Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Konstantinos Katsanos, MD, PhD, MSc, EBIR; Stavros Spiliopoulos, MD, PhD; Panagiotis Kitrou, MD, PhD; Miltiadis Krokidis, MD, PhD; Dimitrios Kanabatidis, MD, PhD

Background—Several randomized controlled trials (RCTs) have already shown that paclitaxel-coated balloons and stents significantly reduce the rates of vessel restenosis and target lesion revascularization after lower extremity interventions.

Methods and Results—A systematic review and meta-analysis of RCTs investigating paclitaxel-coated devices in the femoral and/or popliteal arteries was performed. The primary safety measure was all-cause patient death. Risk ratios and risk differences were pooled with a random effects model. In all, 28 RCTs with 4663 patients (89% intermittent claudication) were analyzed. All-cause patient death at 1 year (28 RCTs with 4432 cases) was similar between paclitaxel-coated devices and control arms (2.3% versus 2.3% crude risk of death; risk ratio, 1.08; 95% CI, 0.72–1.61). All-cause death at 2 years (12 RCTs with 2316 cases) was significantly increased in the case of paclitaxel versus control (7.2% versus 3.8% crude risk of death; risk ratio, 1.86; 95% CI, 1.15–2.97; number-needed-to-harm, 25 patients [95% CI, 19–59]). All-cause death up to 5 years (3 RCTs with 863 cases) increased further in the case of paclitaxel (14.7% versus 8.1% crude risk of death; risk ratio, 1.93; 95% CI, 1.27–2.93; number-needed-to-harm, 14 patients [95% CI, 9–32]). Meta-regression showed a significant relationship between exposure to paclitaxel (dose-time product) and absolute risk of death (0.4±0.1% excess risk of death per paclitaxel mg-year; P=0.001). Trial sequential analysis excluded false-positive findings with 99% certainty (2-sided α, 1.0%).

Conclusions—There is increased risk of death following application of paclitaxel-coated balloons and stents in the femoropopliteal artery of the lower limbs. Further investigations are urgently warranted.

Clinical Trial Registration—URL: www.crd.york.ac.uk/PROSPERO. Unique identifier: CRD42018099447. (J Am Heart Assoc. 2018;7:e011245. DOI: 10.1161/JAHA.118.011245)

Key Words: balloon angioplasty • paclitaxel • paclitaxel-coated balloon • paclitaxel-eluting stent
Meta-Analyses on Similar Pools of Industry Randomized Data

<table>
<thead>
<tr>
<th>Mortality Risk Ratio (RR) or Hazard Ratio (HR)</th>
<th>Independent Randomized Data</th>
<th>Observational Data</th>
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</thead>
<tbody>
<tr>
<td>[paclitaxel devices to non-paclitaxel devices]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR 1.93</td>
<td></td>
<td></td>
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<tr>
<td>RR 1.72</td>
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<td>RR 1.57</td>
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<td>HR 1.38</td>
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<td>HR 1.27</td>
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<td>Pre-Vital Status Update</td>
<td>May 2019</td>
<td>Aug 2019</td>
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<tr>
<td>JAHA1</td>
<td>FDA1,2</td>
<td>VIVA/NAMSA4,5</td>
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<td>863 yrs</td>
<td>971 yrs</td>
<td>1,035 yrs</td>
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<tr>
<td>4-5 yrs</td>
<td>≤ 5 yrs</td>
<td>≤ 5 yrs</td>
</tr>
<tr>
<td>2,185 yrs</td>
<td>med.</td>
<td>med.</td>
</tr>
<tr>
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<tr>
<td>4.8 yrs</td>
<td>4 yrs</td>
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</table>

Available at Panel 2019
Updated since Panel 2019
New series since Panel 2019

2. FDA Executive Summary, Circulatory System Devices Panel Meeting, Figure 14 June 19-20, 2019; pre vital status.
3. Whalley E, FDA presentation, Circulatory System Devices Panel Meeting, Gaithersburg, MD June 19, 2019; post vital status.
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>
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<td>48/3340</td>
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<tr>
<td>PES</td>
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<td>138/6283</td>
<td>78/4263</td>
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<td>6771</td>
<td>139/6730</td>
<td>72/4041</td>
<td>38/2340</td>
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</table>

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

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

**TLR Frequency**

TLR Rates of DES in the SFA are NOT the same as the Coronary Bed


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**

<table>
<thead>
<tr>
<th>Endovascular modalities</th>
<th>Drug release</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Coated Stent</td>
<td>FAST</td>
</tr>
<tr>
<td>Drug Eluting Stent</td>
<td>CONTROLLED/SUSTAINED</td>
</tr>
<tr>
<td>Drug Eluting Balloon</td>
<td>FAST</td>
</tr>
<tr>
<td>Drug “Coated” Balloon</td>
<td>FAST</td>
</tr>
</tbody>
</table>

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

Arterial Paclitaxel Concentration (ng/mg)

Time (Days)

Typical DCB Curve

IMPROVE EFFICACY
(overlap restenotic cascade)

Typical DES Curve

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
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 days

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

SELUTION SLR™ Sirolimus-Eluting Balloon with Sustained Release (CE-Marked)

Presented by A. Finn, CRT 2022

1. Drug concentration evident in MicroReservoirs and tissue - Data on file at M.A. Med Alliance SA
vehicle.

SELUTION SLR & CAT are trademarks of M.A. Med Alliance SA - © 2021 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)

**Drug Dose per Balloon Size**

En Face Scanning Electron Microscope at 24 hours


Medtronic – Presentation R. J. Melder (LINC 2012)

Bard – Catheterization and Cardiovascular Interventions 83:132-140 (2014)
## MEDALLIANCE Sponsored 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>SELUTION FIM SFA/Popliteal</td>
<td>50</td>
<td>Germany</td>
<td>Single Arm</td>
<td>2 Year Data</td>
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<tr>
<td>SELUTION4SFA SFA/Popliteal</td>
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<td>Europe/US</td>
<td>RCT</td>
<td>Enrolling</td>
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<tr>
<td>JAPAN SFA SFA/Popliteal</td>
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<td>Japan</td>
<td>Single Arm</td>
<td>12 Month Data</td>
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<tr>
<td>CHINA SFA SFA</td>
<td>139</td>
<td>China</td>
<td>RCT</td>
<td>Enrolling</td>
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<tr>
<td>SUCCESS PMS SFA/BTK/Foot</td>
<td>772</td>
<td>Asia/Europe/LAM</td>
<td>Single Arm</td>
<td>Enrolling</td>
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<tr>
<td>SELUTION4BTK BTK</td>
<td>377</td>
<td>Europe/US</td>
<td>RCT</td>
<td>Enrolling</td>
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</table>

## Physician-Initiated Trials

<table>
<thead>
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<th>Region</th>
<th>Design</th>
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<tbody>
<tr>
<td>PRESTIGE</td>
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<td>Asia</td>
<td>Single Arm</td>
<td>24 Month Data</td>
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<tr>
<td>PRISTINE</td>
<td>BTK</td>
<td>Asia</td>
<td>Single Arm</td>
<td>12 Month Data</td>
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<tr>
<td>STEP</td>
<td>Foot</td>
<td>Austria</td>
<td>Single Arm</td>
<td>Completed</td>
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<tr>
<td>FLOW</td>
<td>SFA</td>
<td>Germany</td>
<td>RCT</td>
<td>1 Month Data</td>
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</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), Yoshimitus Soga²)

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

## OBJECTIVES
- To assess the safety and efficacy of the SELUTION SLR DEB in treatment of stenosis or occlusion of SFA and/or PA in patients with Rutherford category 2-4

## DESIGN
- Prospective, controlled, multi-center, open, single-arm clinical investigation
- 134 subjects in 13 sites in Japan

## PRIMARY ENDPOINT
- Primary Endpoint: primary patency of the target lesion – **12M**
- Primary patency defined as freedom from clinically driven TLR and freedom from restenosis as determined by DUS (PSVR≥2.5)

## FOLLOW-UP
- 30 days, 6, 12, 24 and 36 months post-procedure

## PIs
- Osamu Iida
- Yoshimitsu Soga
SELUTION SFA JAPAN - Efficacy outcomes

Primary Endpoint – 12M Primary Patency

87.9%

Days post index Procedure
0 180 365
Numbers at risk 134 126 114
Primary patency: freedom from clinically driven TLR and freedom from restenosis as determined by DUS (PSVR≥2.5)
O. Iida, LINC 2023

Secondary Endpoint – 12M freedom from TLR

97.0%

Days post index Procedure
0 180 365
Numbers at risk 134 131 125
O. Iida, LINC 2023
First Time Data Release at LINC

SUCCESS PMS update
Results from the first 321 patients enrolled

Tue 6 JUN @15:40
ROOM 4- Speakers’ Corner

Performance of a novel Sirolimus eluting balloon in peripheral arterial disease: Insights from the SUCCESS PTA study

Michael Lichtenberg
Klinikum Hochsauerland, Arnsberg, Germany
First Time Data Release at LINC

LIMUS FLOW

Tue 6 JUN @ 16:15
ROOM 4- Speakers’ Corner

Vascular effects through Sirolimus vs. Paclitaxel DCB treatment in symptomatic peripheral artery disease – the Limus FLOW investigator-initiated randomized controlled trial

Christos Rammos
Universitätsmedizin Essen Germany
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

0,083 0,5 1 3 24 72 168 336 720

1 hour 24 hours 3 days 7 days 14 days 30 days 60 days 90 days 120 days

Treated Segment Iliofemoral

Sirolimus ng/g

0 200 400 600 800 1000 1200 1400 1600

0 100 200 300 400 500 600 700

Sirolimus ng/g

1 hour 24 hours 3 days 7 days 14 days 30 days 60 days 90 days 120 days

Courtesy: Alok 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
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 | All N=50 | Femoropopliteal N=20 (% or range) | Below the knee N=30 (% or range)
--- | --- | --- | ---
Primary patency | 80.0% | 88.2% | 74.0%
DEBATE BTK DUEL

**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.

- **Patients:** 172
  - **Enrolled:** 76

FUTURE SFA- ASIA

**PI:** Prof. Edward Choke

Sponsored, Randomised, Double blind, Multicentres (186 SCB : 93 PTA) To determine the effectiveness (primary patency) of Magic Touch versus standard percutaneous transluminal angioplasty for the treatment of superficial and popliteal arterial disease.

- **Patients:** 279
  - **Enrolled:** 56

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.

- **Patients:** 219
  - **Enrolled:** 78
DEBATE BTK Duell

Dr. Francesco Liistro,
Chief of Interventional cardiology
San Donato Hospital - Arezzo, Italy

- **Study Objective:** The objective of this study is to compare the remote patency of the sirolimus (Magic Touch) vs. paclitaxel (Lithos) release balloon, in patients undergoing tibial artery revascularization.

- **Study Design:** Randomized, controlled, open, multicentre, prospective study. Block randomization with paclitaxel medicated balloon or Sirolimus medicated balloon (1:1).

- **Study Population:** Assessment of non-inferiority and superiority (in terms of late vascular lumen loss by calculating 6-month Late Luminal Loss and 12-month vessel reocclusion) of the sirolimus-releasing flask compared to the paclitaxel-dedicated flask.
**FUTURE-SFA**

- Subject target: 279
- Rutherford class 3-6
- SFA, P1, P2
- Single or sequential lesion, 2-20cm
- De novo or re-stenosis lesion
- No significant inflow dis
- At least 1 patent crural artery run-off to foot

- Determine effectiveness (primary patency)

- Quadruple blinded (Participants, care provider, investigator, outcome assessor)

- 2:1 enrollment

- CRO controlled

- Core Lab adjudicated

- Follow-up 6, 12, 24 months

**FUTURE-BTK**

- Subject target: 219
- Rutherford class 4-6
- Proximal 20cm of BTK arteries
- Single or sequential lesion, 2-20cm
- De novo or re-stenosis lesion
- No significant inflow dis
- Target vessel has run-off to foot after Rx
Real World Outcomes of Sirolimus Coated Balloons vs Plain Balloon Angioplasty in CLTI Patients: Insights from HOPE Prospective Registry

Edward Choke

Tue 6 JUN @14:10
Room 1: Main Arena
**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

1132 Patients
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 infrainguinal angioplasty to prevent one-year major adverse limb events in a representative population (‘all-comers’) of patients with PAD

1132 Patients
830 Patients Enrolled
SirPAD

Major adverse limb events in patients with femoro-popliteal and below-the-knee peripheral arterial disease treated with either sirolimus-coated balloon or standard uncoated balloon angioplasty.
Study Objective: evaluate whether the use of sirolimus-coated balloon catheters is non-inferior to uncoated balloon catheters in infra-inguinal angioplasty to prevent one-year major adverse limb events, including unplanned major amputation of the target limb and target lesion revascularization to treat critical limb ischemia, in a representative population (`all-comers`) of patients with PAD.

Study Design: RCT, all comers, single centre.

Study Population: 1132 patients (566 per study arm) allow to show non-inferiority of the intervention group with a power of 80% and a type I error rate of $\alpha=2.5\%$ one-sided. Assuming a drop-out rate of approximately 5%, a total of 1200 patients will be randomized in the study.
Head-to-Head Comparison of \textit{Siro}limus versus Paclitaxel Drug-Eluting Balloon Angioplasty in the Femoropopliteal Artery
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
**MATSA - Spain**

**PI:** Dra. Claudia Riera; Co-PI: Dr. Marc Sirvent

Investigator-initiated, Prospective, single arm, multicenter study to assess the safety and efficacy of the Magic Touch for the treatment of femoropopliteal lesions in subjects with PAD

**150 Patients**
20 Patients Enrolled

**LIMES - Germany**

**PI:** Dott. Ulf Teichgräber

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

**250 Patients**
67 Patients Enrolled
UPCOMING CLINICAL TRIALS - PTA

MAGICAL BTK - IDE FDA

- PI: 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

Primary Endpoints

Safety Endpoint @ 6 months:
MALE+POD

Efficacy Endpoint @ 12 months:
Primary Patency + Limb Salvage

5-Year Follow-Up

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

2nd and 3rd Generation Tyrocore BRS

Fantom

Fantom Encore & MOTIV BTK

All Other Players Use Off-the-Shelf Materials

PLLA Used in Surgical Products

Bone Screws
Orthopedic Surgery

Thread
Plastic Surgery

1st Generation PLLA BRS

Absorb

DESolven

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>
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<tr>
<td><strong>Shortening</strong></td>
<td>1% (lengthening)</td>
</tr>
<tr>
<td><strong>Maximum expansion diameter</strong></td>
<td>Size (mm)</td>
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<tr>
<td></td>
<td>2.5</td>
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<tr>
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<td>3.5</td>
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<td>4.0</td>
</tr>
</tbody>
</table>

| **Catheter type**                     | Rapid exchange             |
| **Guide catheter compatibility**      | 6F                         |
| **Working catheter length**           | 139 cm                     |
| **Scaffold lengths**                  | Current 12, 18, 24 mm 36, 48, 60mm |
| **Nominal pressure**                  | 7 atm                      |
| **Rated burst pressure**              | 18 atm                     |
| **Balloon material**                  | Nylon                      |

Courtesy Ehrin Armstrong, MD
**MOTIV™ Bioresorbable Scaffold**

**Preliminary Study Outcomes**

- **99% Technical Success in all patients** (71/72 Scaffolds)

- **Primary Patency**
  - **6-month final result: 90% Patency** \( (N=47 \text{ patients/48 limbs}) \)

- **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

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1. PSVR data for 40 patients (51/52 patients: 47 patients completed 6 month visit): no device related adverse events; PSVR not recorded
2. 79 patients have completed the 12-month follow-up as of 3/28/2023.
The R3 Vascular Drug-Eluting Bioresorbable 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></td>
<td>Mean ± SD or % (Range)</td>
<td></td>
<td></td>
</tr>
<tr>
<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>
<td>2.85 ± 0.37 (2.20 – 3.26)</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>0.68 ± 0.37 (0 – 1.35)</td>
<td>2.95 ± 0.32 (2.25 – 3.45)</td>
<td>2.09 ± 0.68 (0.94 – 2.99)</td>
</tr>
<tr>
<td>Late Lumen Loss (mm)</td>
<td>---</td>
<td>---</td>
<td>0.57 ± 0.55 (-0.23 – 1.31)</td>
</tr>
<tr>
<td>Diameter Stenosis (%)</td>
<td>78.74 ± 10.83 (62.71 – 100)</td>
<td>14.31 ± 6.89 (3.90 – 27.88)</td>
<td>28.27 ± 16.86 (8.28 – 57.27)</td>
</tr>
<tr>
<td>Binary Restenosis (% , n)</td>
<td>---</td>
<td>---</td>
<td>11.1% (1)*</td>
</tr>
</tbody>
</table>

**In-Segment Analysis**

- *57% DS by core lab, asymptomatic, not treated*
Temporary Spur Stent System

SPUR Stent:
- Self Expanding Nitinol Frame w/integrated balloon
- Re-Capturable
- Available in 2 diameters (OD): 3mm, 4mm*
- Treatment Length ≈ 60mm
- Gold Radiopaque Markers
Reflow Medical’s Temporary Spur Stent System*

• 6F compatible sheath system
• Self-expanding temporary uncoated/drug-coated nitinol stent on a balloon system
• Spikes enable controlled penetration of vessel calcification
• Deeper drug delivery
• Uncoated, artery channel creation
• Coated, drug deposited in artery channels
• Minimize recoil & dissections
• Minimal drug loss during transit (covered)
• Intended to deliver stent-like results while leaving nothing behind

*Under Clinical Investigation

**FIRST TIME DATA RELEASE:**
DEEPER OUS trial: 6 months results with the bare temporary spur stent system in conjunction with paclitaxel coated balloons
Michael Lichtenberg
14:15-14:20
Room 1 – Main Arena

Currently being conducted OUS: DEEPER OUS and DEEPER LIMUS studies

Received FDA Breakthrough Designation: anticipated trial in 2022
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.
• The next 3 years will herald a new era in peripheral arterial drug delivery technology.