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

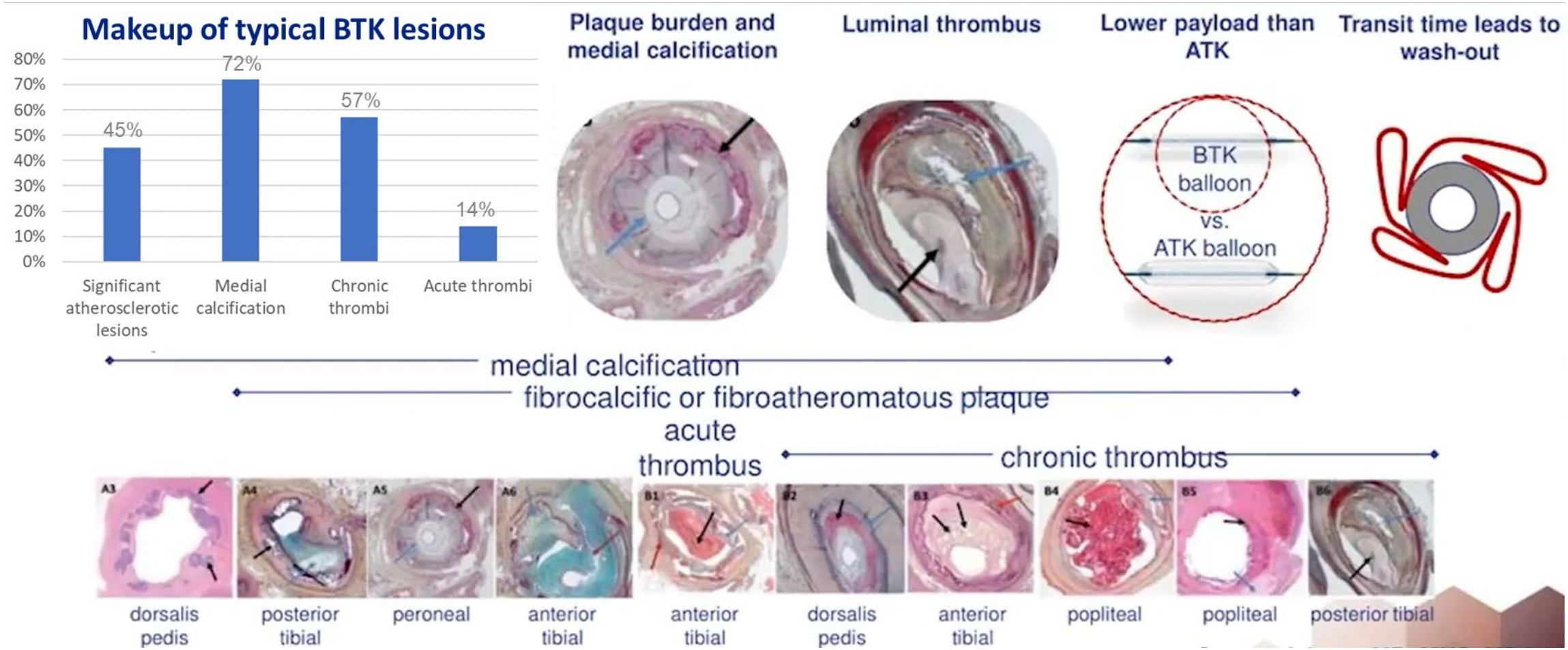
Previous experience with DCB in BTK
A Series of Negative Studies

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

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

Adapted from G. Adams, VIVA 2020

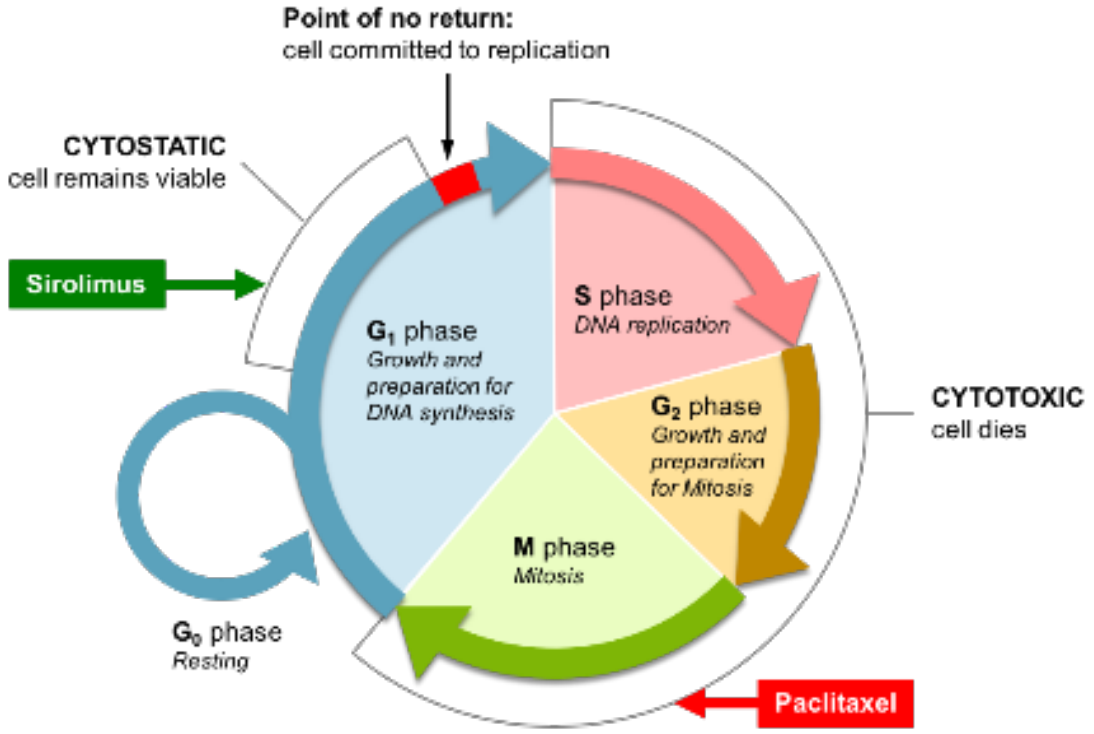
BTK Challenge for Intimal Drug Delivery: Barrier Tissue



Narula, et al. JACC 2018;72:2152-63

Sirolimus' Unique Pharmacokinetic Profile

- Potent antiproliferative agent, prevents activation of SMC's after vascular injury
- Powerful immunosuppressive agent, prevents inflammation and reduces cell injury by inhibiting inflammatory cells
- Cell anti-migratory agent, stops activated SMC's from detaching from matrix and moving into the surface of the endothelium
- Maintains cells in G0 resting phase and limits apoptosis



Dumont, F. J., & Su, Q. (1996). *Life sciences*, *58*(5), 373–395.

Paclitaxel and Sirolimus

Similar but different

ANTI-RESTENOTIC

CYTOSTATIC

10'000 FOLD
SAFETY MARGIN

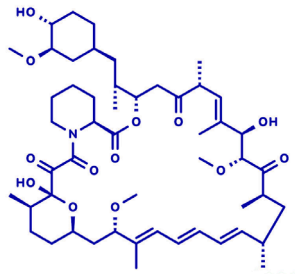
WIDE
THERAPEUTIC RANGE

ANTI-INFLAMMATORY

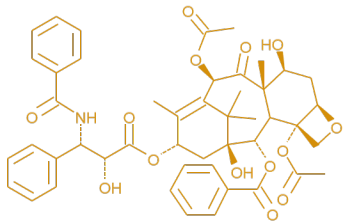
LOW
TISSUE ABSORPTION

SHORT
TISSUE RETENTION

Both are **antiproliferative agents**.
They **inhibit smooth muscle cells** and **endothelial cells** proliferation and migration,
however
auxiliary pharmacological properties are considerably different



Sirolimus



Paclitaxel

ANTI-RESTENOTIC

CYTOTOXIC

100 FOLD
SAFETY MARGIN

NARROW
THERAPEUTIC RANGE

X

FAST
TISSUE ABSORPTION

LONG
TISSUE RETENTION

Wessely, Rainer et al. *JACC*, vol 47, no. 4, 2006, pp. 708-714.

Sirolimus Eluting Balloon Design Goals

What is needed to address technological challenges related to the use of limus in DCB?

- **INCREASE DRUG UPTAKE**
  - Difficult to get Sirolimus to enter the arterial tissue within 30 to 180 seconds of balloon dilatation; hence some kind of **"instant glue"** required to transfer the drug from the balloon to the tissue efficiently

- **EXTEND DRUG RETENTION**
  - Sirolimus must be continuously delivered over time, so some form of **"time release mechanism"** must be employed to maintain therapeutic levels

- **LIMIT DRUG EMBOLIZATION**
  - Protect from WASH-OFF during balloon delivery and to **protect from EMBOLIZATION during balloon deployment**

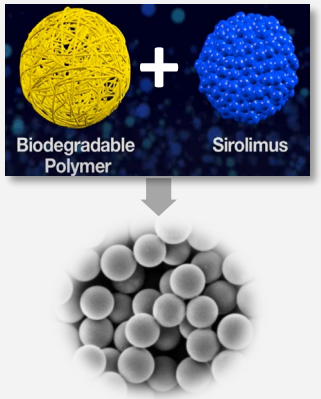
Presented by A. Finn, CRT 2022

SELUTION SLR™ Sirolimus-Eluting Balloon

Latest Generation of Drug-Eluting Balloons

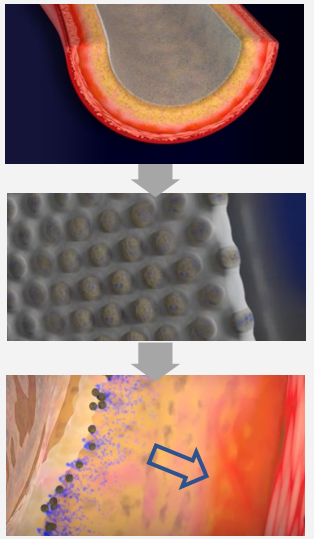
MicroReservoirs made from **biodegradable polymer** intermixed with **molecular Sirolimus drug**:

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



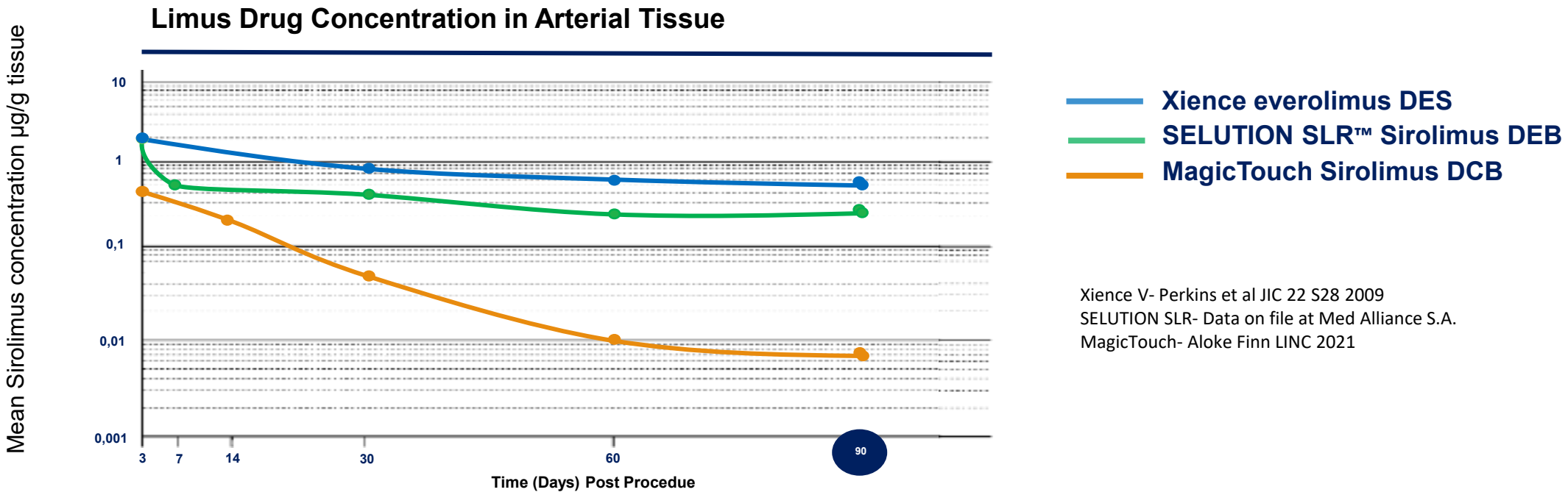
Proprietary Cell Adherent Technology – CAT™ :

- 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 resulting in DES like Pharmacokinetics

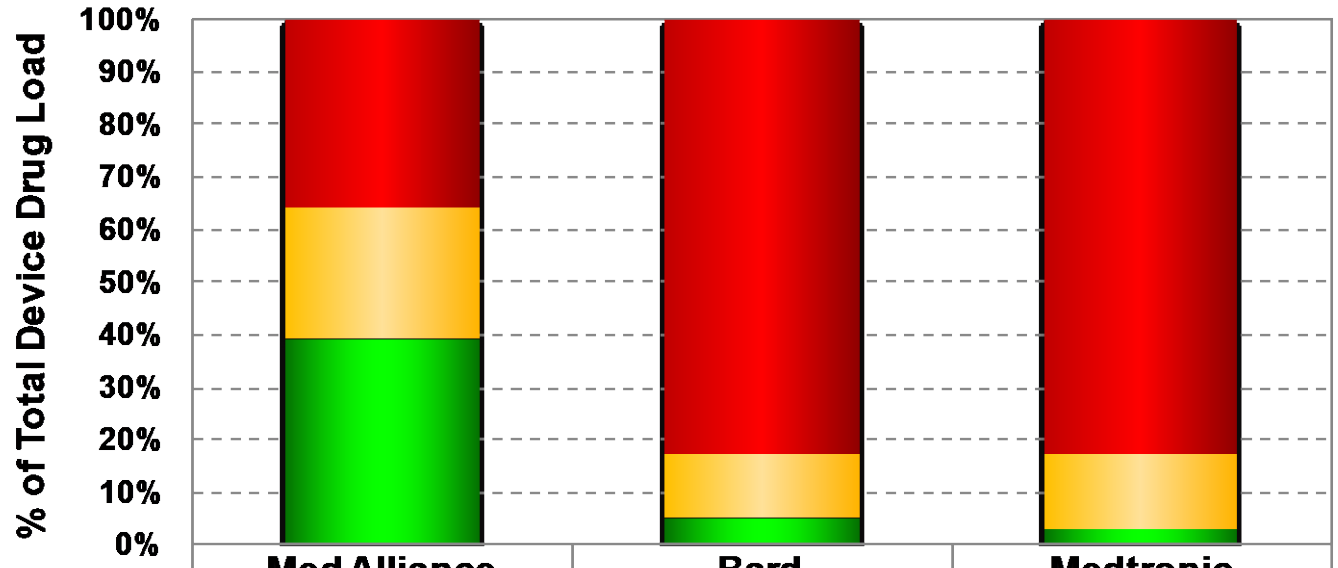
- **MicroReservoirs ensure a controlled** and **sustained** Sirolimus drug release to maintain **therapeutic effect** in tissue over long period of time and up to 90 days[1]



Xience V- Perkins et al JIC 22 S28 2009
SELUTION SLR- Data on file at Med Alliance S.A.
MagicTouch- Aloke Finn LINC 2021

SELUTION™ vs. Competition

Drug Transfer



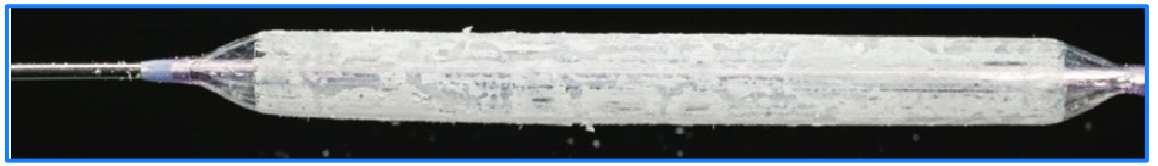
	Med Alliance SELUTION	Bard LUTONIX	Medtronic IN.PACT
Lost during procedure	36%	83%	83%
Retained on balloon	25%	12%	14%
Transferred to vessel (1 hr)	39%	5%	3%

Med Alliance – Bench Test Data on File / Bard-LUTONIX & Medtronic-IN.PACT – Presentation Granada at CRT 2014.

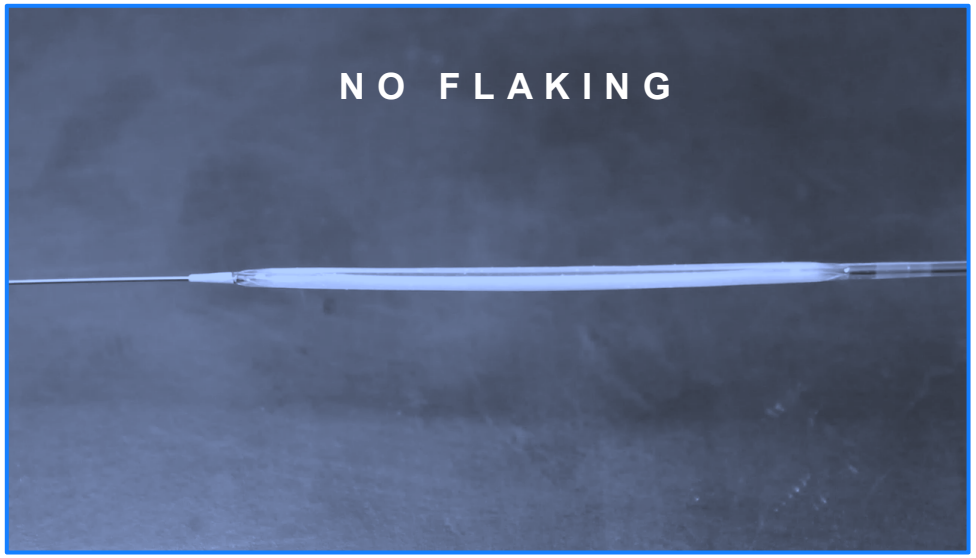
Proprietary Balloon Coating Technology - CAT™

Improved Coating Integrity

Competitor A
with crystalline coating
(Paclitaxel)



SELUTION SLR™

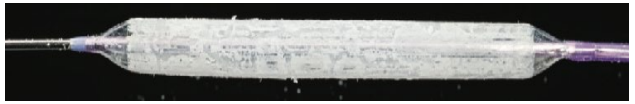


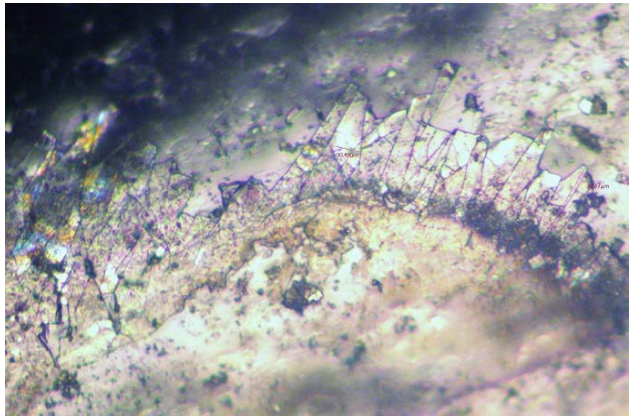
Proprietary Balloon Coating Technology - CAT™

Deliverability

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

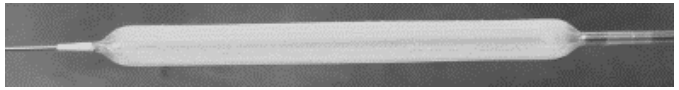
Medtronic IN.PACT™

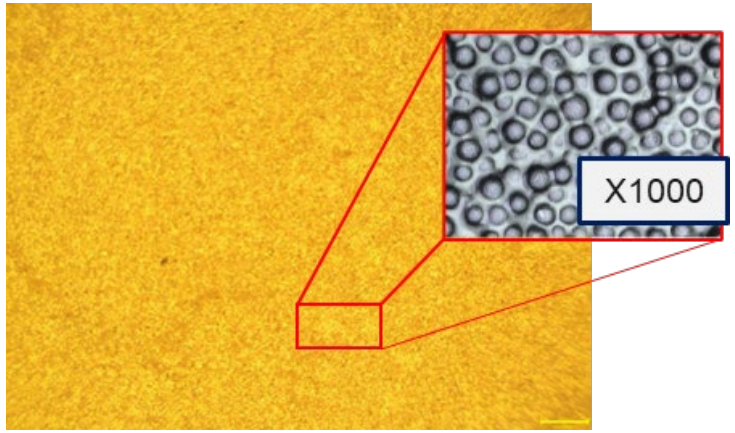




100x, Medtronic IN.PACT

SELUTION SLR™





100x, SELUTION SLR

(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

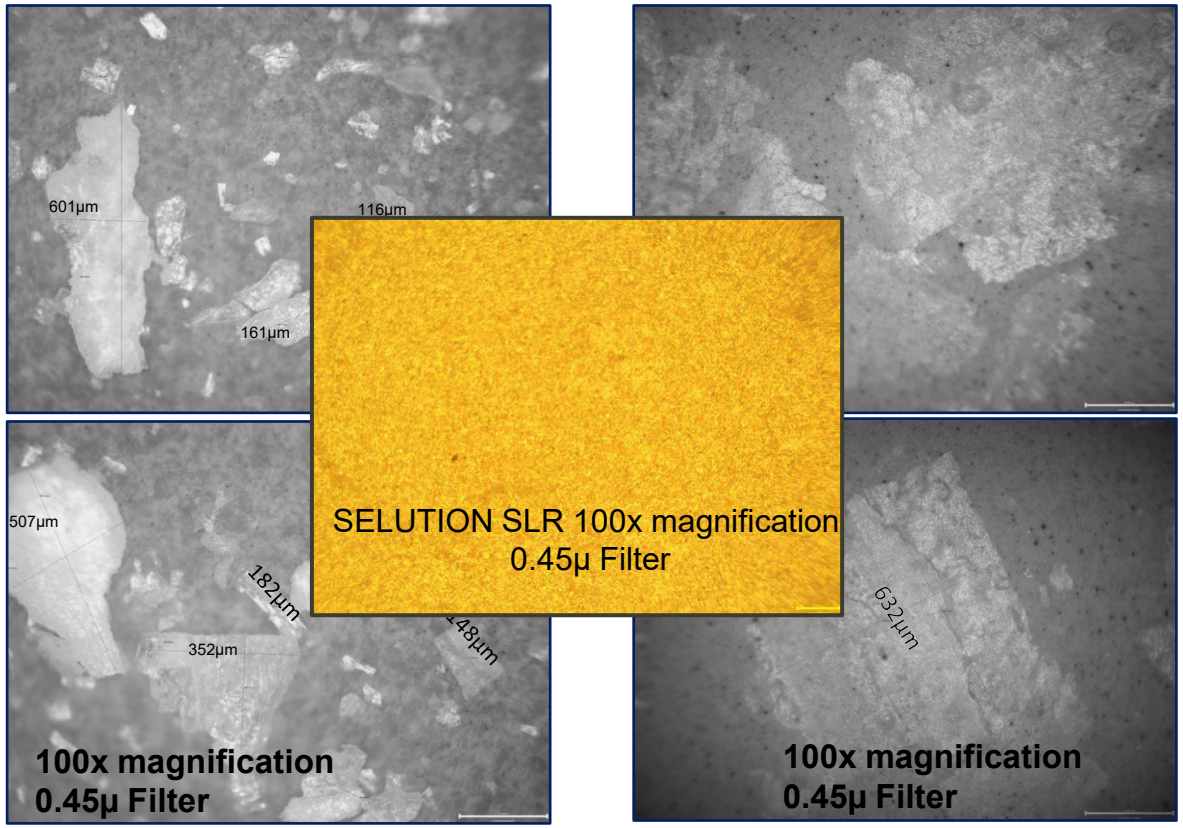
Comparison with Crystalline Coatings

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 Program

A Global Program with over 7000 patients involved

SFA

+920 patients

SELUITON4SFA IDE/ Enrolling
(300 pts, 60 sites)
NCT05132361
SELUTION FIM (50 pts, 4 sites)
SFA JAPAN (134 pts, 14 sites)
SUCCESS PM (722 pts, 29 sites)
(50% SFA, 50% BTK)
LIMUS FLOW (70 pts)

#BTK

+850 patients

SELUTION4BTK IDE- Enrolling
(376 pts, 60 sites)
NCT05055297
PRESTIGE (BTK) (25 pts)
PRISTINE (BTK) (75 pts)
STEP (Foot trial) (20 pts)
SUCCESS (722 pts, 29 sites)
(50% SFA, 50%BTK)

#AVF

+420 patients

AVF IDE (300 pts, 40 sites)
ISABELLA (40 pts)
SAVE (84 pts, 3 sites)

#Coronary ISR

+420 patients

SELUITON4ISR IDE- Enrolling
(418 pts, 60 sites)
NCT04280029
ISR FIM ~10 patients, 6 sites

#DeNovo

+4,900 patients

SELUTION4 De Novo SV IDE – Site Selection
(960 pts, 80 sites)
NCT05946629
SELUTION FIM (50 pts, 6 sites)
Chinese Bifurcation study (280 pts, 10 sites)
SELUTION DeNovo (3326 pts, 60 sites)
LOVE DEB (300 pts, 10 sites)

#ED

+60 patients

SELUTION FIM ED (10 pts)
ED MDR PERFECT (54 pts)

SELUTION SLR - Clinical Trial Program

Peripheral Program ~ 2'000 Patients

SelutionSLR™ SUSTAINED LIMUS RELEASE

MedAlliance Sponsored Trials	Indication	Patient Numbers	Region	Design	Status
SELUTION FIM	SFA	50	Germany	Single Arm	Completed 2 Year Data
SUCCESS – Post Market Registry	SFA/Popliteal/ Tibial/Pedal	772	Asia/Europe/LAM	Single Arm	Enrolling
SELUTION4SFA – IDE FDA trial	SFA/Popliteal	300	US&Canada/Europe/Asia	RCT	Enrolling
SELUTION4BTK – IDE FDA trial	BTK	377	US/Europe/Asia	RCT	Enrolling
JAPAN SFA	SFA	134	Japan	Single Arm	Completed 1 Year Data
CHINA SFA	SFA	139	China	RCT	Enrolling

Physician-Initiated Trials	Indication	Patient Numbers	Region	Design	Status
PRESTIGE	BTK	25	Asia	Single Arm	24 Month Data
PRISTINE	BTK	75	Asia	Single Arm	12 Month Data
STEP	Foot	20	Austria	Single Arm	Enrolling
FLOW	SFA	70	Germany	RCT	Completed 1 Month Data

Early experience with SELUTION SLR in BTK

PRESTIGE (N=25) – 24 mo FU available

ClinicalTrials.gov ID: NCT04071782

OBJECTIVES	• 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
DESIGN	• Prospective, non-Randomized single-center trial, single arm • Treatment of 25 patients from Asia
PRIMARY ENDPOINTS	• Freedom from device-or procedure-related mortality through 30 days • Freedom from target lesion revascularization (TLR)at 6 months and 12 months
SECONDARY ENDPOINTS	• Freedom from major target limb amputation • Primary patency rate at 6 and 12M • Technical success (ie, able to cross and dilate lesion to achieve <30% residual stenosis) • Clinical success (ie, improvement of Rutherford classification at follow-up) • Wound healing(ie, complete closure of wound / >70% healed)

PRISTINE (N=75) – 12 mo FU available

ClinicalTrials.gov ID: NCT04534257

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

Tjun Yip Tang and Tze Tec Chong, Singapore General Hospital

PRESTIGE & PRISTINE

Data in summary

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 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 rate: **79.2%**

Tjun Yip Tang and Tze Tec Chong, Singapore General Hospital

SELUTION4BTK Trial

Selution 4 BTK
FDA Study

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) • 376 patients (min 50% in USA) • 60 sites in USA, Europe, Singapore, Hong Kong & New Zealand
PRIMARY ENDPOINTS	• Efficacy: Hierarchical composite efficacy endpoint determined by Win Ratio method 6 months post-procedure according to the following hierarchy of outcomes: Major (Above-ankle) amputation, CD-TLR , Target lesion occlusion, Transverse View Area Loss (TVAL%) by angiography. • Safety: Freedom from the composite of Major Adverse Limb events (MALE) & and all-cause perio-operative death (POD) at 30 days
FOLLOW-UP	• 1, 6 months • 1, 2, 3, 4, 5 years
PIs	• US: Ehrin Armstrong • EU: Marianne Brodmann

SELUTION4BTK Trial

Enrolling sites*

*Current site list EU, Asia, NZ
Site selection process ongoing

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

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

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

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

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

Austria
- LKH – Universitaets Klinikum Graz (M. Brodmann)

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

New Zealand
- Auckland City Hospital (A. Holden)

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

Greece
- Patras University Hospital (K. Katsanos)

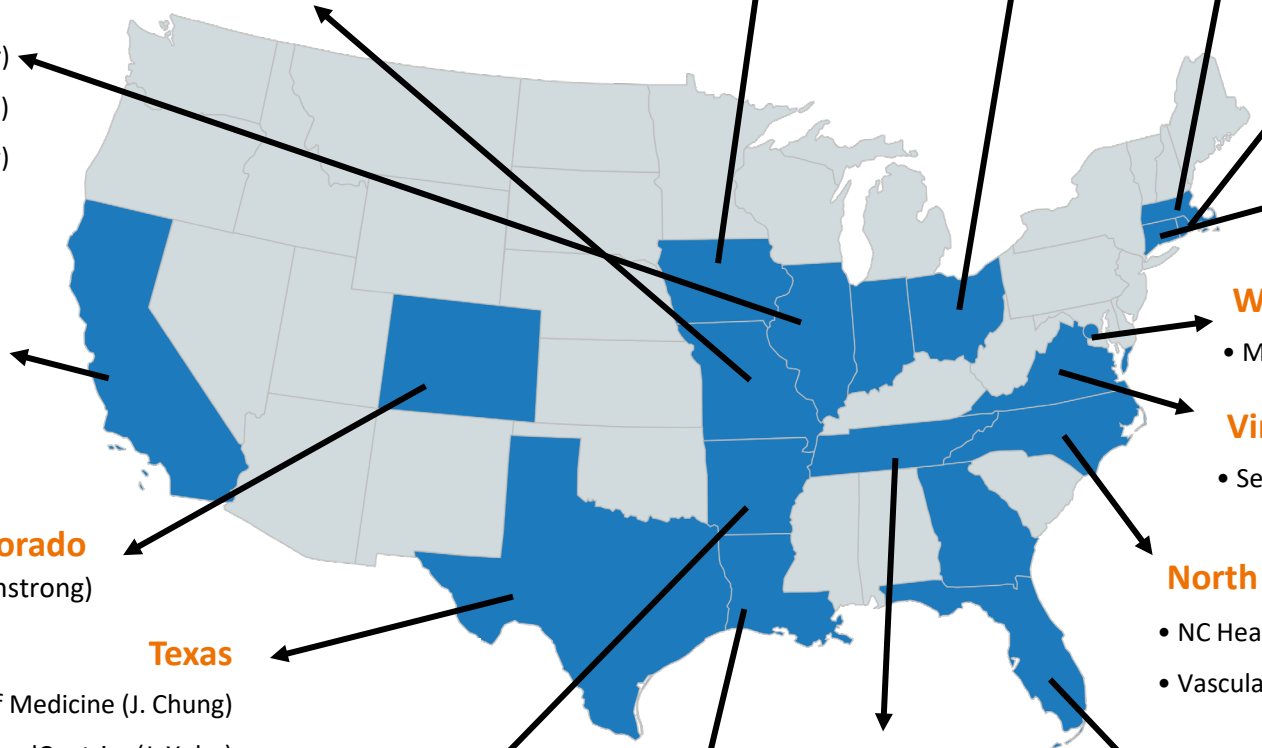
Selution 4 BTK
FDA Study

SELUTION4BTK Trial

Enrolling sites*

*Site selection process ongoing

Selution 4 BTK
FDA Study



Ohio
- Cleveland Clinic (A. Khalifeh)

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

Iowa
- Vascular Institute of the Midwest (E. Dippel)

Missouri
- Saint Luke's Hospital (S. Laster)

Illinois
- Advocate Aurora Research Institute (J. Golzar)
- Advocate Lutheran General Hospital (L. Schwartz)
- Rush University Medical Center (S. Madassery)

Rhode Island
- Miriam Hospital (P. Soukas)

Connecticut
- Yale University (C. Mena)

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

Washington, DC
- Medstar Health Research Institute (N. Bernardo)

Virginia
- Sentara Norfolk General Hospital (S. Steerman)

Colorado
- ClinRé (E. Armstrong)

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

Texas
- Baylor College of Medicine (J. Chung)
- WoundCentrics (J. Yoho)

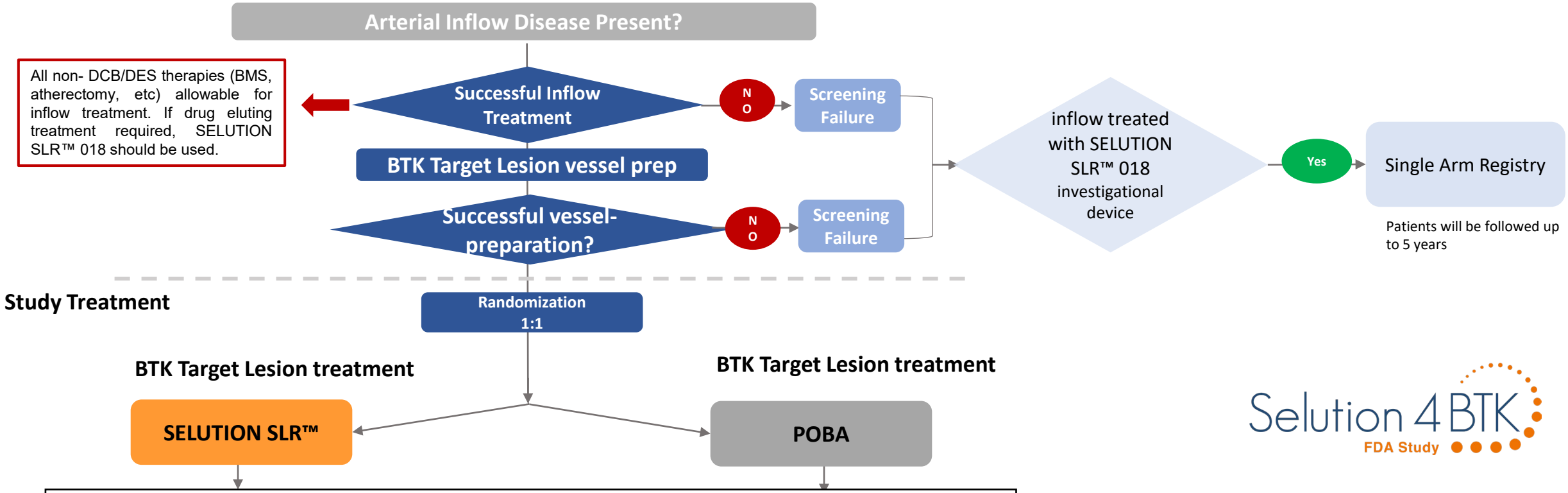
Arkansas
- Arkansas Heart Hospital (V. Lendel)
- St. Bernards Medical Center (B. Tedder)

Tennessee
- Vanderbilt University Medical Center (D. Clair)
- Tennessee Center for Clinical Trials (D. Gupta)

Florida
- Palm Vascular Center (R. Beasley)
- Cardiac and Vascular Institute Research Foundation (A. Lee)
- Memorial Healthcare System (J. Roberts)

Louisiana
- Cardiovascular Institute of the South (C. Walker)

SELUTION SLR™ BTK-IDE study



Selution 4 BTK
FDA Study

- Clinical Follow –up : 1 month, 6 months, 12 months and then yearly out to 5 years
- Angiographic Follow up : 6 months

Primary endpoints:

- **Efficacy:** Hierarchical composite efficacy endpoint determined by Win Ratio method according to the following hierarchy of outcomes: Major (Above-ankle) amputation, CD-TLR , Target lesion occlusion, Transverse View Area Loss (TVAL%) by angiography at 6 months.
- **Safety:** Freedom from the composite of Major Adverse Limb events (MALE) & and all-cause perio-operative death (POD) at 30 days

Conclusions

- **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 and 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!