Bioresorbable scaffolds for BTK-reconstructions: Is there a future?

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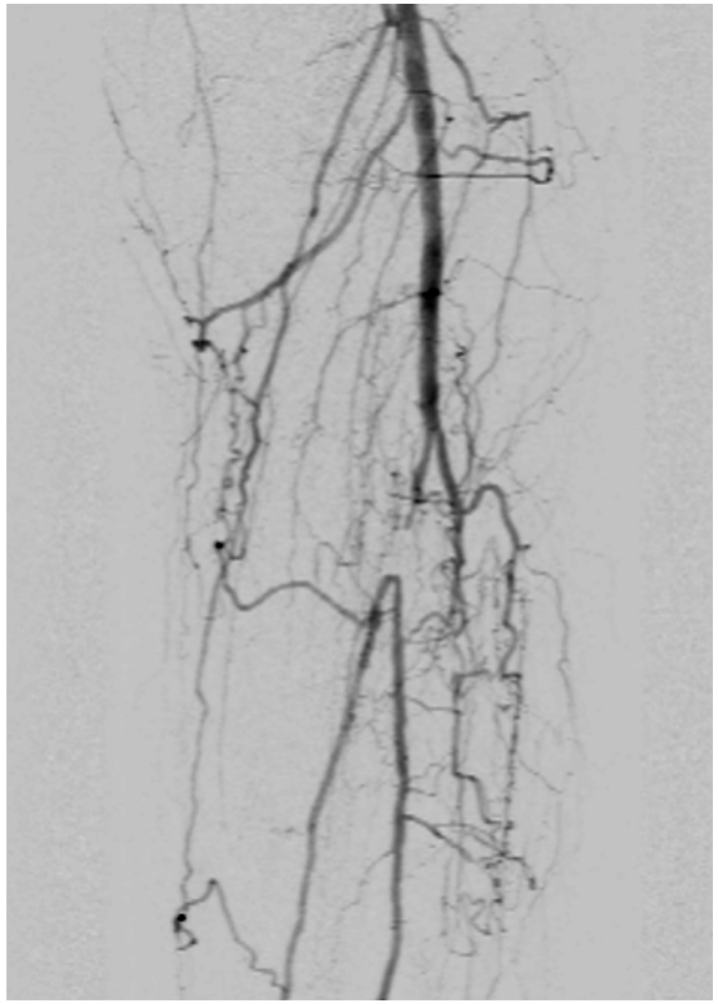
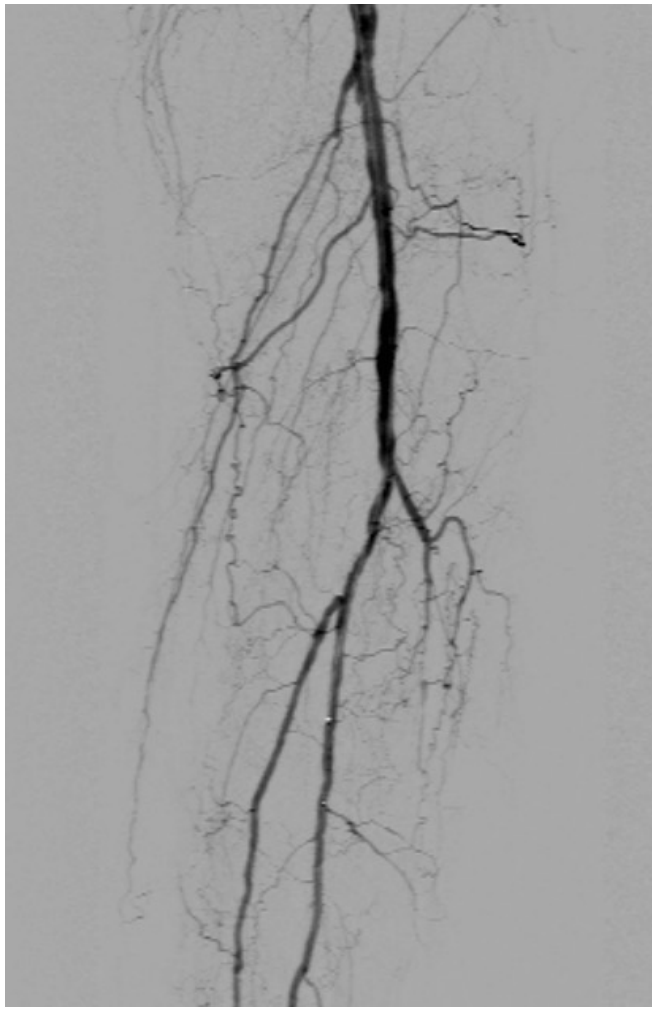
Disclosure Statement of Financial Interest

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

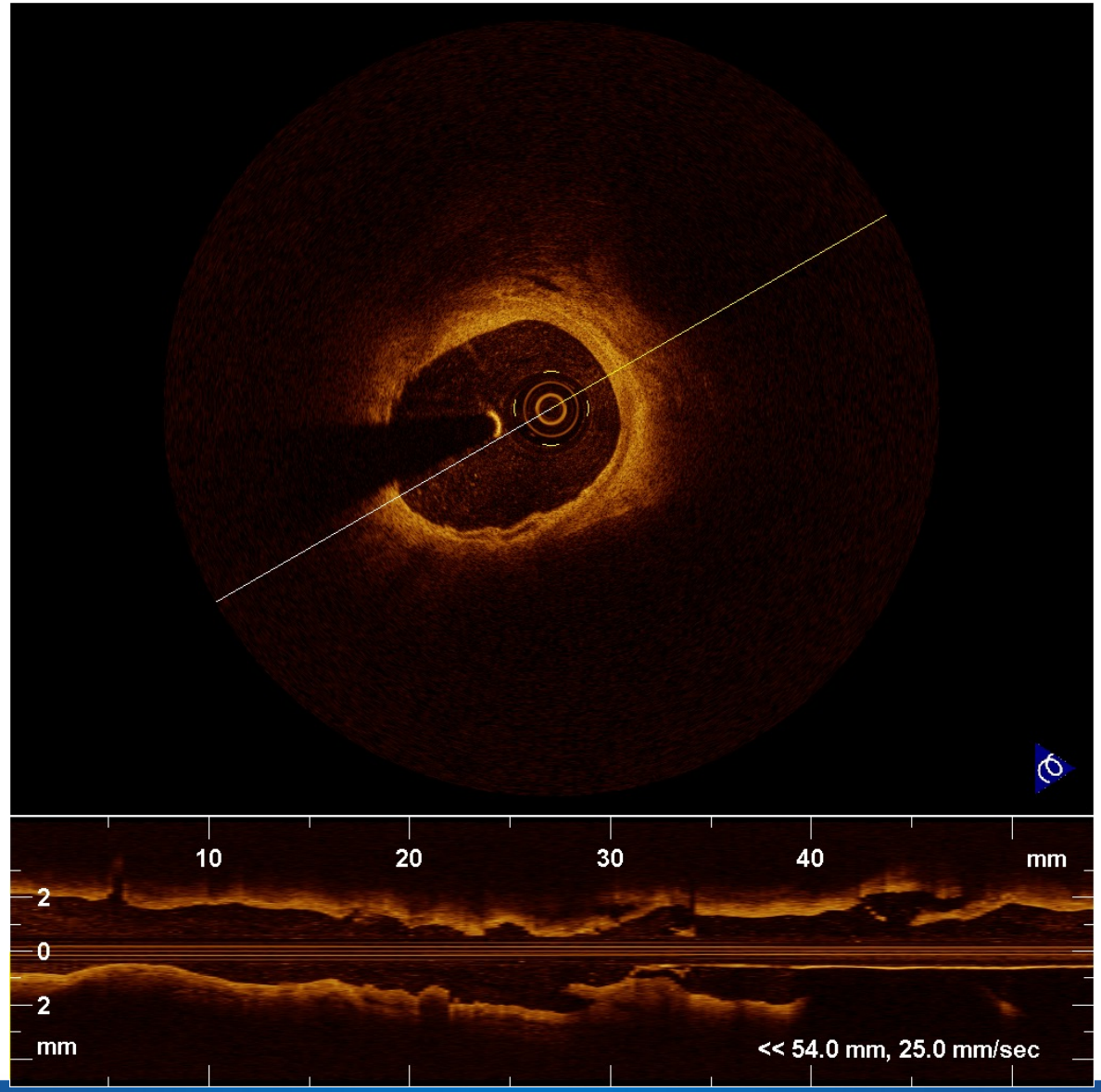
Affiliation/Financial Relationship	Company
• ***Institutional Research Support***	• **Shockwave Medical, TriReme Medical, Surmodics, Abbott (Global PI), Boston Scientific (DSMB), Veryan Medical, Acotec**
• ***Advisory Board***	• **Abbott, Janssen, Medtronic, Boston Scientific, CSI, Philips**
• ***Consulting***	• **Terumo, Abiomed, Penumbra, Inari, Canon**

Short Segment Occlusion PTA: Satisfactory Angiographic Result?



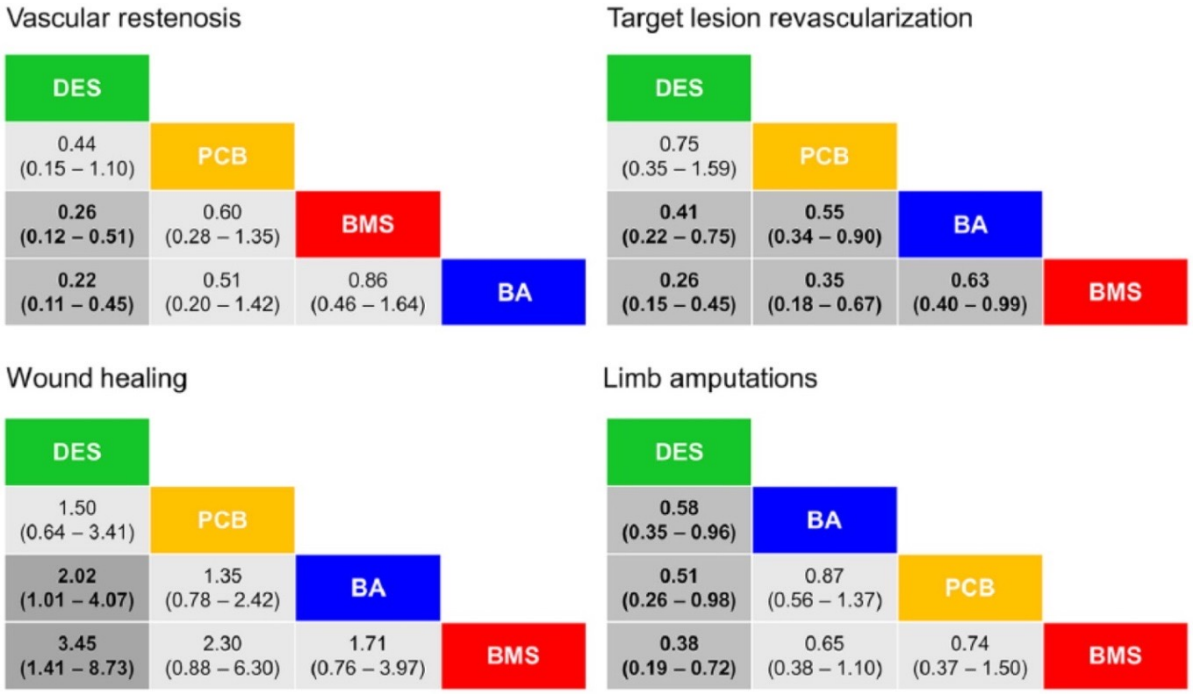


OCT of TP Trunk Post PTA



CLI & BTK Interventions

- Below-the-knee interventions are generally reserved for patients with CLI[1]
- Meta-analysis of endovascular treatment for infrapopliteal artery disease:[2]
  - "Infrapopliteal **DES were associated with significantly lower rates of restenosis, TLR, and amputations and improved wound healing** compared to BA and BMS. **DES also significantly reduced amputations** compared with paclitaxel-coated balloons."

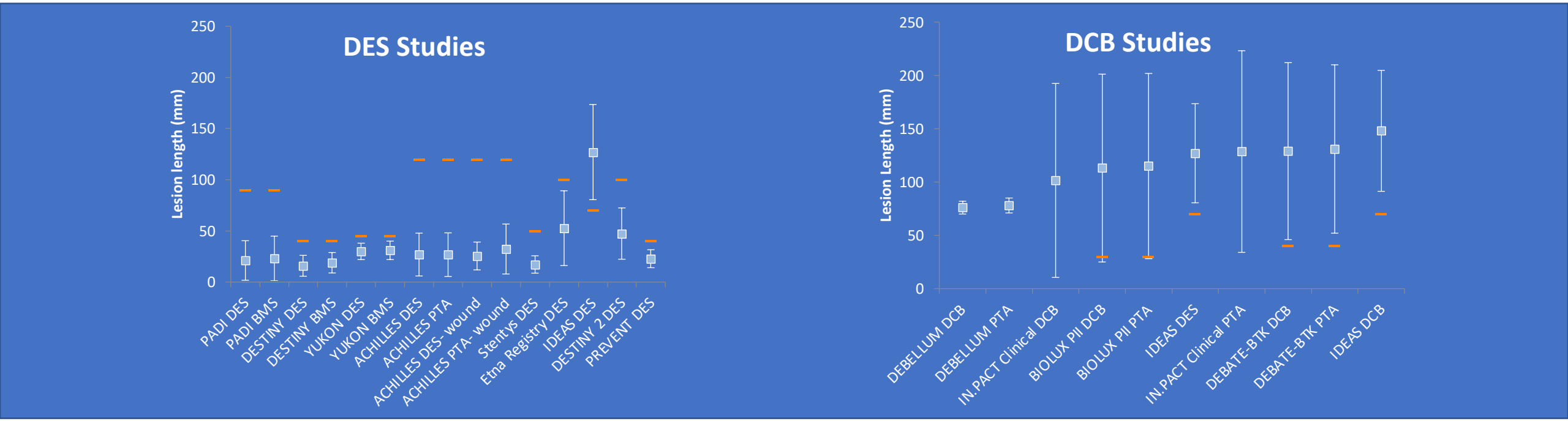


Hierarchical matrices of pairwise comparisons for all competing treatments as generated by a Bayesian binomial random effects model with informative heterogeneity and vague treatment priors. Numbers represent odds ratios and 95% credible intervals. Significant pairwise differences have been highlighted.

BA, balloon angioplasty; BMS, bare metal stent; DES, drug-eluting stent; PCB, paclitaxel-coated balloon.

1. Jaff MR, et al. Ann Vasc Dis. 2015;8(4):343-57.
2. Katsanos K, et al. J Endovasc Ther. 2016;23:851-863.

BTK Interventions (DES & DCB) Lesion Length



Orange lines in graphs are inclusion criteria length max (DES) or min (DCB).

- Target lesion length limited by treatment modality in previous studies

ACHILLES- Scheinert D, et al. J Am Coll Cardiol. 2012;60(22):2290-5.
ACHILLES wound- Katsanos K, et al. JACC Cardiovasc Interv. 2016;9(3):259-67.
BIOLUX PII- Zeller T, et al. JACC Cardiovasc Interv. 2015;8(12):1614-22.
DEBATE-BTK- Liistro F, et al. Circulation. 2013;128:615-621.
DEBELLUM- Fanelli F, et al. J Cardiovasc Surg (Torino). 2014;55(2):207-16.
DESTINY 2- Bosiers M, et al. J Cardiovasc Surg (Torino). 2017;58(1):49-54.
DESTINY- Bosiers M, et al. J Vasc Surg. 2012;55(2):390-8.
Etna Registry- Giaquinta A, et al. Vasc Endovascular Surg. 2017;51(2):60-66.

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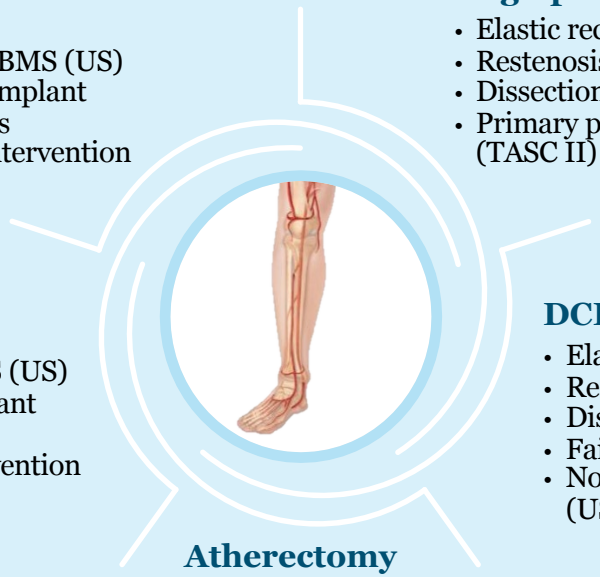
Etna Registry- Giaquinta A, et al. Vasc Endovascular Surg. 2017;51(2):60-66.

Current endovascular treatment options for BTK

Current treatment options for tibial circulation*

BMS
- Restenosis
- No on-label BMS (US)
- Permanent implant
- Short lengths
- Surgical reintervention

Angioplasty
- Elastic recoil
- Restenosis
- Dissection
- Primary patency 20%–50% (TASC II)



DES
- No on-label DES (US)
- Permanent implant
- Short lengths
- Surgical reintervention

DCBs
- Elastic recoil
- Residual plaque
- Dissection
- Failed RCTs
- No approved DCB (US)

Atherectomy
- Device variability
- Embolization
- Lack of data

To effectively treat BTK disease*

	Drug (inhibit NIH)	**Scaffold** (minimize recoil)	**Leave nothing behind**
Angioplasty	✗	✗	✓
Atherectomy	✗	✗	✓
BMS	✗	✓	✗
DES	✓	✓	✗
DCB	✓	✗	✓
Ideal Treatment	✓	✓	✓

*Adapted from Varcoe R. Long term results and a glimpse into the future with bioresorbable scaffolds for BTK? Presented at The Leipzig Interventional Course (LINC). January 28–31, 2020.

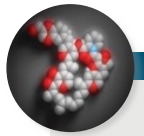
COLUMBIA NewYork-Presbyterian

BMS = bare metal stent; DCB = drug-coated balloon; DES = drug-eluting stent; NIH = neointimal hyperplasia; RCT = randomized controlled trial; TASC = Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Arterial Disease.

Treatment hypothesis is driving a new therapy: drug-eluting resorbable scaffolds (DRS)

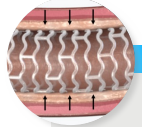
To effectively treat BTK disease

	Inhibit NIH	Minimize recoil & repair dissections	Leave nothing behind
Ideal treatment	✓	✓	✓



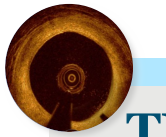
DRUG

Inhibit restenosis and provide drug-modulated healing for sustained patency



SCAFFOLD

Provide transient support in the vessel to address recoil and dissections



TEMPORARY

Resorbable scaffold

Base foundation required for BTK treatment

ANGIOPLASTY

A perfect PTA is the foundation for optimizing lumen gain

1st Gen Absorb Bioresorbable Vascular Scaffold

SCAFFOLD

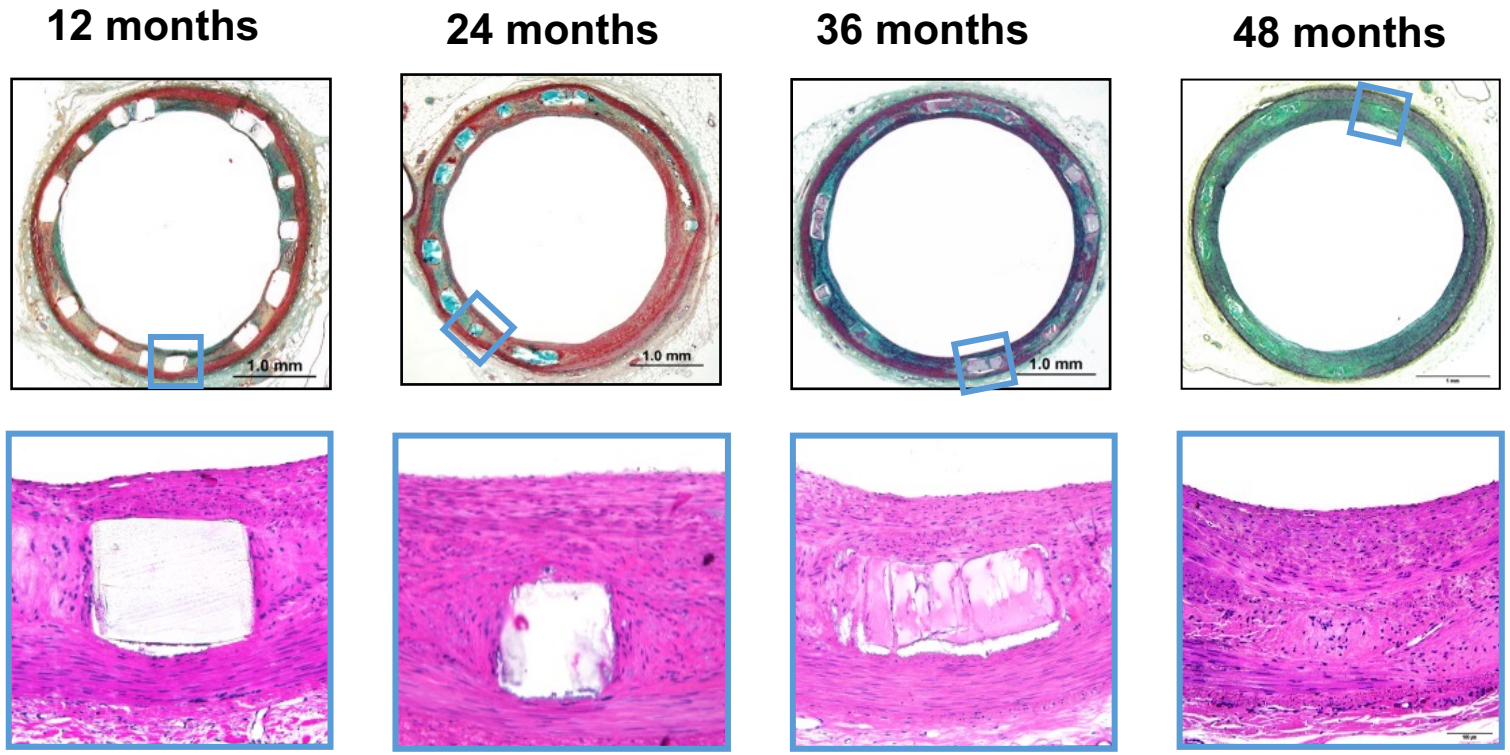
- PLLA Scaffold
- Semi-crystalline
- Provides device structure
- Processed for required radial strength
- Fully resorbs*

DRUG

- Everolimus
- Cytostatic drug

DRUG COATING EXCIPIENT

- poly(D,L-lactide) (PDLLA)
- Thin layer
- Amorphous (non-crystalline)
- Conformal coating, 2-4 µm thick
- Controls drug release
- Fully resorbs



Degrading polymer is replaced by an increasingly cellular provisional matrix.

Representative photomicrographs of porcine coronary arteries implanted with Absorb BVS.
Top: Movat's pentachrome, Bottom: Hematoxylin and eosin, 20x objective
Images on file with Abbott Vascular.

* Platinum markers as proximal and distal ends remain for angiographic visualization

CLI/BTK EVIDENCE DRS ABSORB BTK

Complete imaging and clinical FU assessment over 5 years

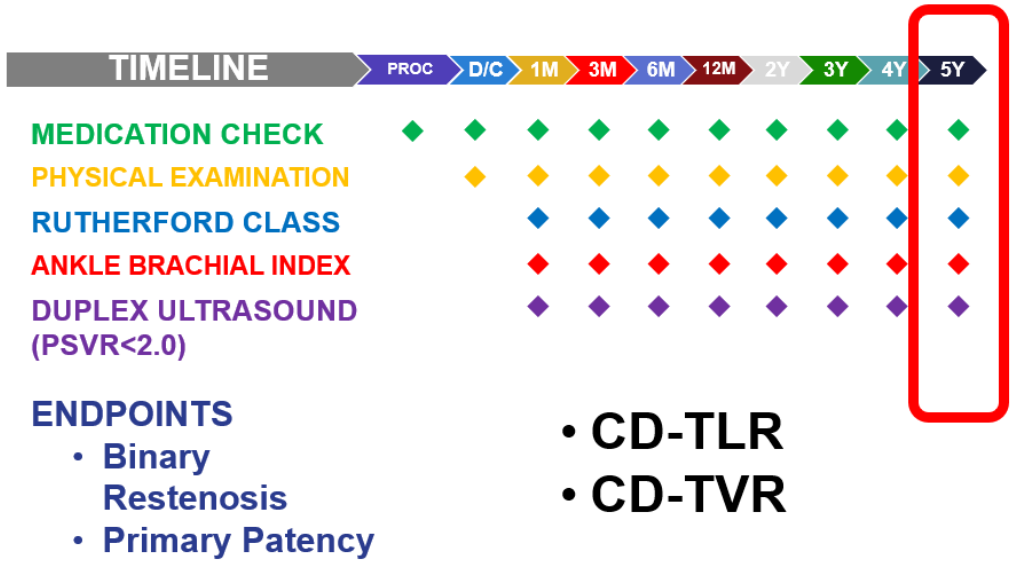
STUDY DESIGN

Prospective, non-randomized, single-center study

Inclusion criteria:

- Chronic lower limb ischemia: RC 3-6
- Life expectancy >1 yr.
- Single or multiple de novo lesions; >60%
- Infrapopliteal arteries (distal P3)
- Total lesion length ≤5cm (Max 2xBVS)
- Diameters 2.5–4.0 mm

STUDY ENDPOINTS



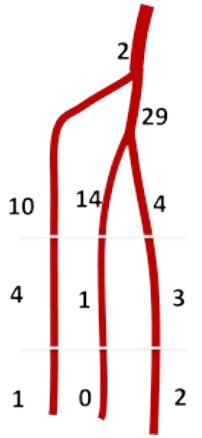
Varcoe et al. 2019.

Absorb in BTK | 5 Year Results

Dr. Ramon Varcoe (single center study)

PATIENT CHARACTERISTICS	
Number of patients	**48**
Gender (male : female)	56% : 44%
Mean Age	82 yrs
Rutherford Score 3	27%
Rutherford Score 4	2%
Rutherford Score 5	60%
Rutherford Score 6	11%
Diabetes	23%

LESION CHARACTERISTICS	
Limbs Treated	**55**
Scaffolds Implanted	**71**
Location of implanted stents:	
• Popliteal (distal third)	2 (2.8%)
• Anterior tibial artery	15 (21.1%)
• Posterior tibial artery	9 (12.7%)
• Tibioperoneal trunk	29 (40.8%)
• Peroneal artery	15 (21.1%)
Mean lesion length	20.1 mm
Range	(5-50 mm)
Mean diameter	3.20 mm
Mean length	25.5 mm

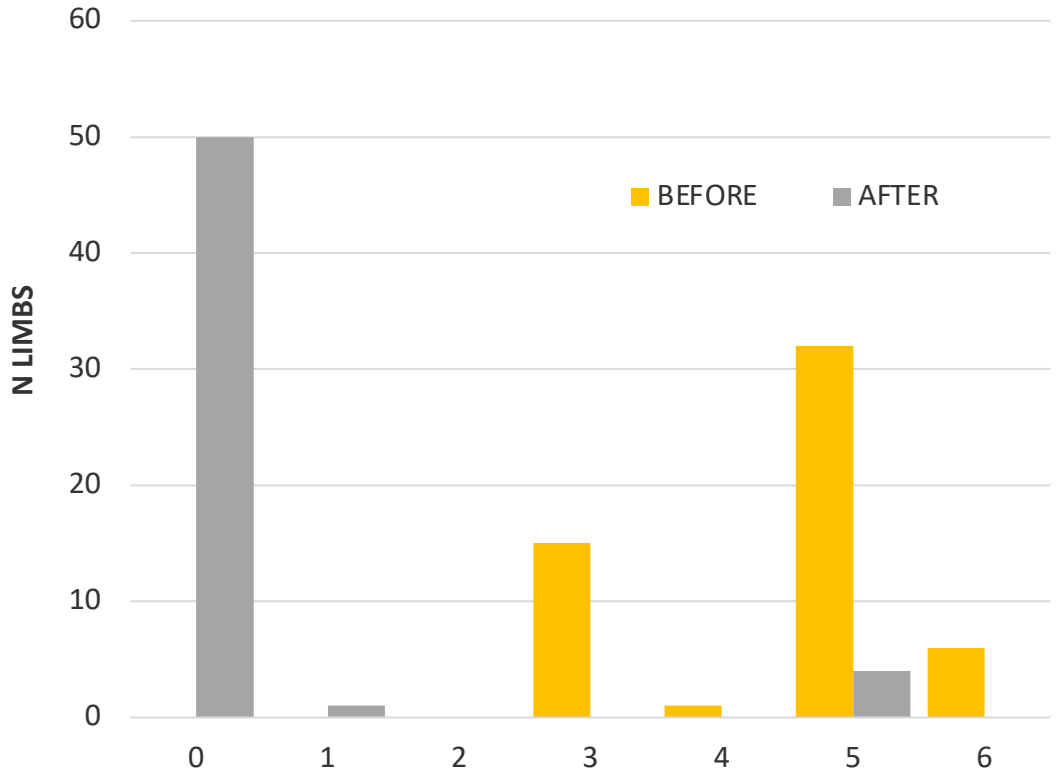


Varcoe RL, et al. Long-term results of a prospective, single-arm evaluation of everolimus-eluting bioresorbable vascular scaffolds in infrapopliteal arteries. Catheter Cardiovasc Interv. 2020 Oct 10. doi: 10.1002/ccd.29327.

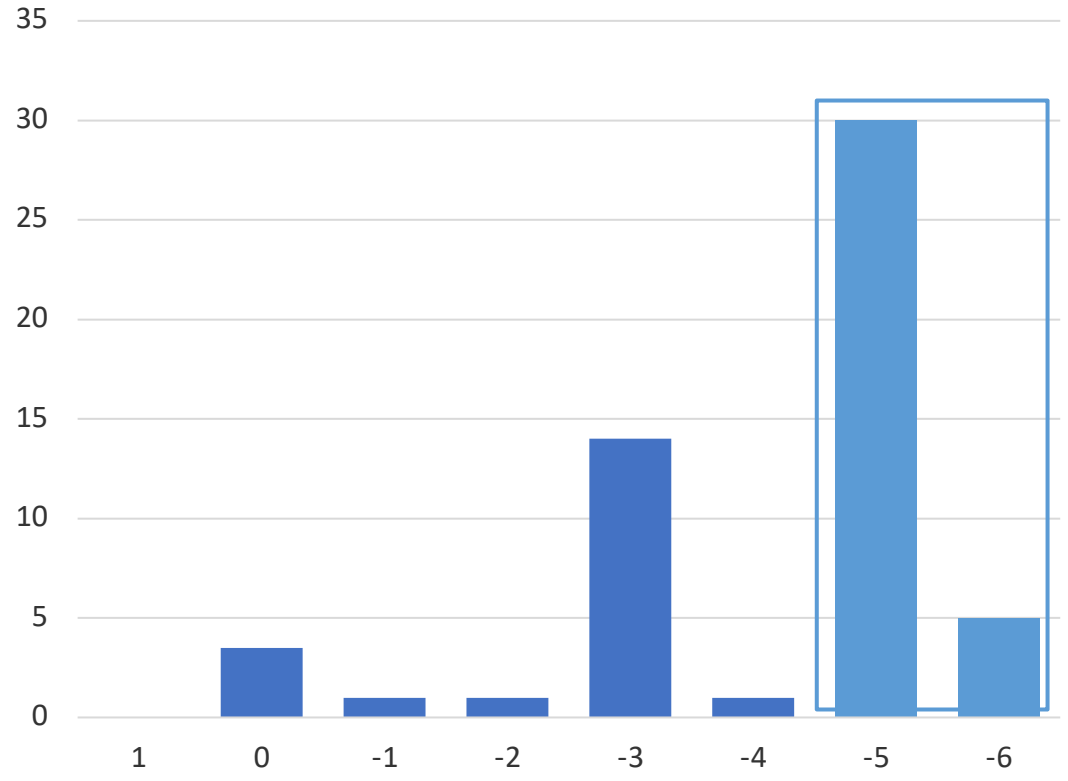
CLI/BTK EVIDENCE DRS

Sustained clinical success over median 35 months of FU

RUTHERFORD-BECKER CLASS

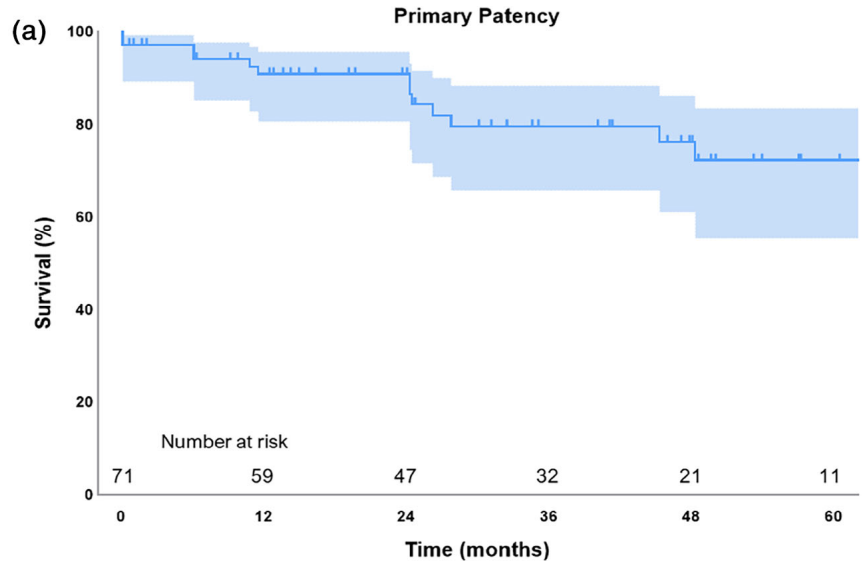


CHANGE IN RUTHERFORD CATEGORY

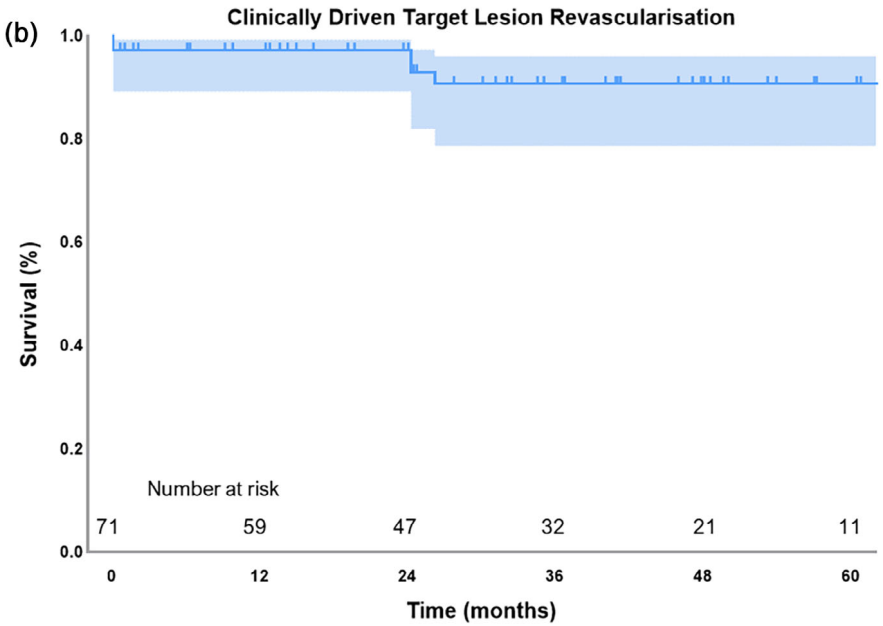


Varcoe et al. 2019.

5 Yr Results with Absorb in BTK Arteries



Primary Patency (%)	100	90.8	90.8	79.7	76.3	72.3
SE (%)	0	3.6	3.6	5.6	6.3	7.1



D-TLR (%)	100	97.2	97.2	90.7	90.7	90.7
E (%)	0	2.0	2.0	4.1	4.1	4.1

Primary Patency

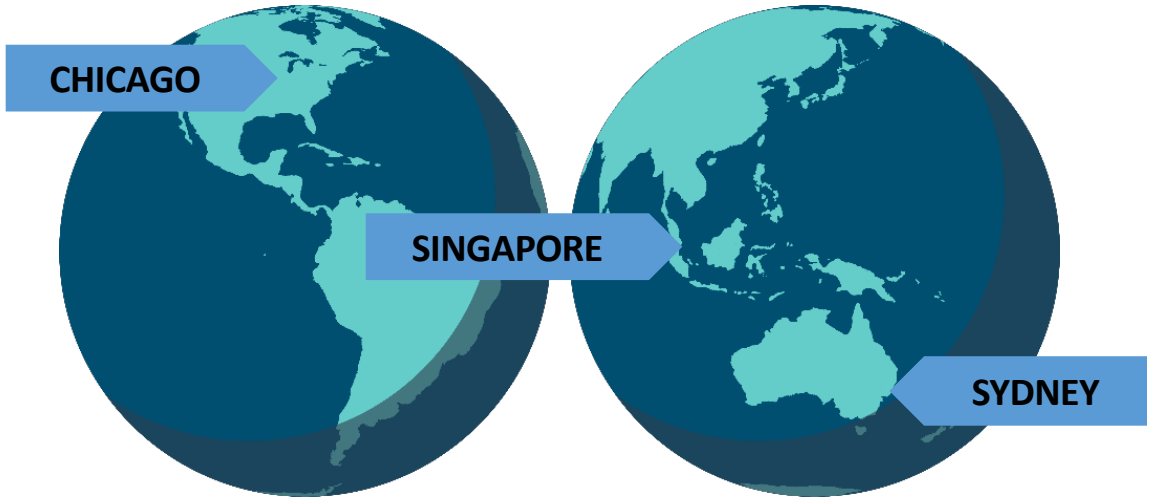
72.3%

Freedom from CD-TLR

90.7%

Varcoe RL, et al. Long-term results of a prospective, single-arm evaluation of everolimus-eluting bioresorbable vascular scaffolds in infrapopliteal arteries. Catheter Cardiovasc Interv. 2020 Oct 10. doi: 10.1002/ccd.29327.

Absorb in BTK: International Pooled Analysis



CONSECUTIVE PATIENTS TREATED WITH ABSORB AUGUST 2012–MAY 2017

INCLUSION:

- Rutherford Class 3–6 CLI
- *De novo* BTK arteries
- Diameter between 2.5 and 4 mm

	NUMBER OF PATIENTS	NUMBER OF LIMBS/LESIONS	NUMBER OF SCAFFOLDS	LENGTH OF FU (TO DATE)
Australia/Varcoe	48	55	71	5y
US/Shah	31	41	49	2y
Singapore/Kum	41	41/53	69	1y

Varcoe et al. Long Term Results and a Glimpse into the Future with Bioresorbable Scaffolds for BTK? LINC 2020.

Absorb in BTK | Pooled Analysis of Three Studies

Majority Were CLI Patients

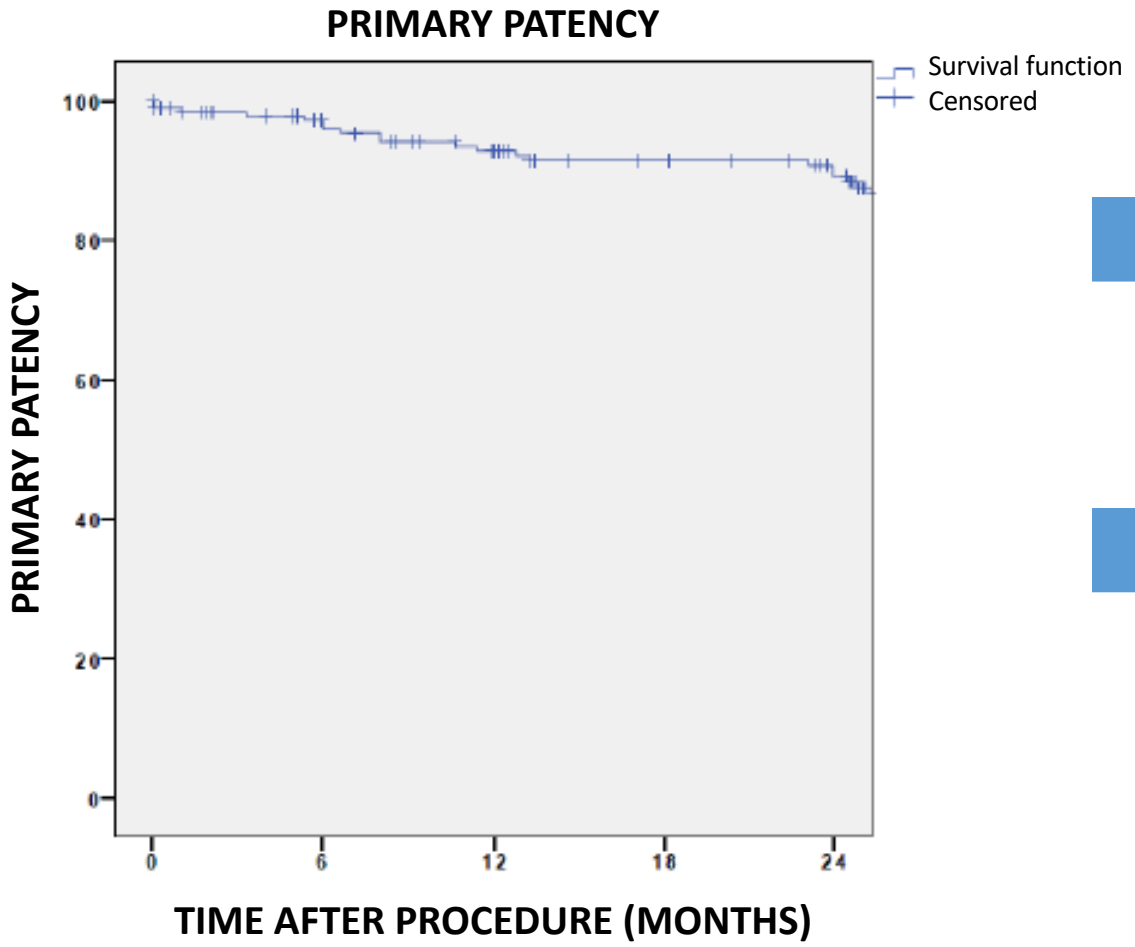
PATIENT CHARACTERISTICS	
Number of patients	**125**
Gender (male : female)	51.2% : 48.8%
Rutherford Score 3	15.7%
Rutherford Score 4	8.7%
Rutherford Score 5	55.9%
Rutherford Score 6	19.7%
TASC A	21.3%
TASC B	15.7%
TASC C	14.2%
TASC D	8.7%
NA	43.3%
Diabetes	55%

LESION CHARACTERISTICS	
Lesions treated	**156**
Location of implanted stents:	
• Popliteal (distal third)	5.51%
• Anterior tibial artery	35.43%
• Posterior tibial artery	36.22%
• Tibioperoneal trunk	33.07%
• Peroneal artery	25.20%
Mean lesion length	25.49 mm
Range	(4-88 mm)
Mean diameter	3.20 mm
Mean length	25.5 mm

Varcoe et al. Long Term Results and a Glimpse into the Future with Bioresorbable Scaffolds for BTK? LINC 2020.

Absorb in BTK | Pooled Analysis of Three Studies

Encouraging Primary Patency and TLR Outcomes



PRIMARY PATENCY	
@ 1y	91.1%
@ 2y	88.6%

FREEDOM FROM TLR	
@ 1y	96.6%
@ 2y	94.5%

Varcoe et al. Long Term Results and a Glimpse into the Future with Bioresorbable Scaffolds for BTK? LINC 2020.

Absorb in BTK | Pooled Analysis of Three Studies

Absorb in BTK Conclusions

- THREE STUDIES WITH ABSORB IN INFRAPOPLITEAL ARTERIES CONDUCTED IN AUSTRALIA, SINGAPORE AND U.S. SHOWED CONSISTENT RESULTS:

100% technical/procedural success

> 80% patency rates and low rates of reintervention @ 1 year

Excellent clinical success and limb salvage rates @ 1 year

Positive results maintained up to 5 years

Varcoe et al. Long Term Results and a Glimpse into the Future with Bioresorbable Scaffolds for BTK? LINC 2020.

Drug-eluting resorbable scaffolds are being investigated as a potential future treatment option for lower limb disease

Company	Device	Scaffold Material	Drug	Status
Abbott	Esprit™ BTK	PLLA	Everolimus	Enrolling in LIFE-BTK Trial (N=225)
Biotronik	Magmaris™	Magnesium	Sirolimus	Completed 24-month data from a single center retrospective study (N=28)
Meril	MeRes™	PLLA	Sirolimus	Enrolling 12-month results from CREDENCE BtK Study (N=30)
Reva	Motiv™	Tyrocore™ (Tyrosine-Derived Polycarbonate)	Sirolimus	CE Mark Enrolling physician-initiated BTK study (N=50)
Efemoral Medical	Efemoral with FlexStep Technology	Unknown	Sirolumus	Enrolling Efemoral I FIH single arm multi-center (n=100) for SFA

This technology provides a scaffold to resist recoil and tack dissections, a drug to inhibit neointimal hyperplasia, and ultimately leave nothing behind (resorbable materials)

New therapy segment name: Drug-eluting Resorbable Scaffold (DRS)

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
225 patients randomized
2:1 Esprit™ BTK vs. PTA

6-MONTH PRIMARY ENDPOINTS

Safety Endpoint:
MALE+POD

Efficacy Endpoint:
Primary Patency + Limb Salvage

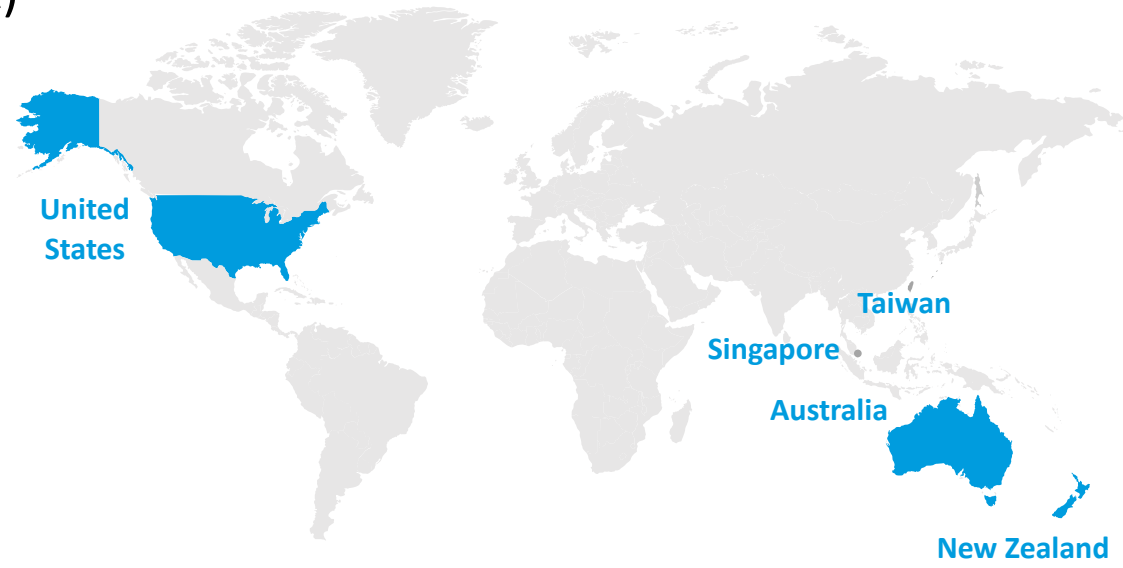
5-YEAR FOLLOW-UP

TRIAL LEADERSHIP

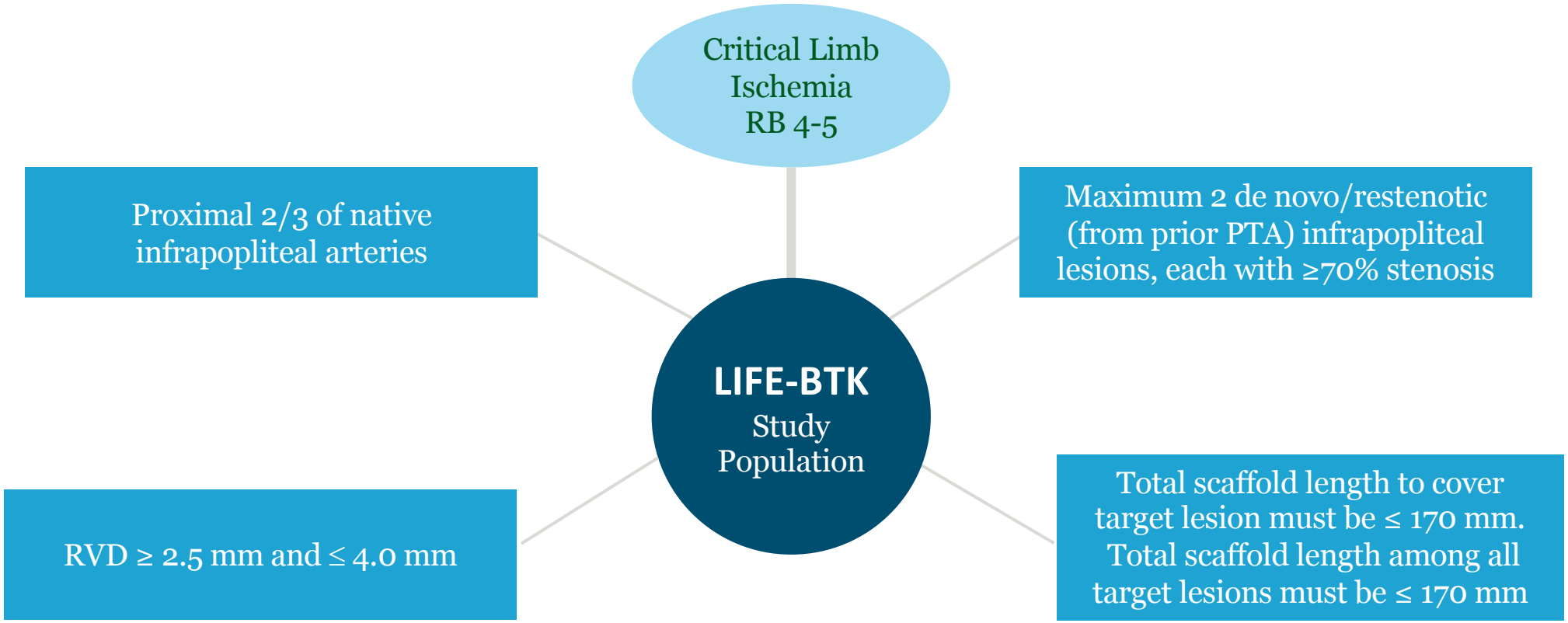
Ramon Varcoe MBBS, MS, FRACS, PhD; Sahil A. Parikh MD, FACC, FSCAI; Brian DeRubertis MD, FACS

Study design

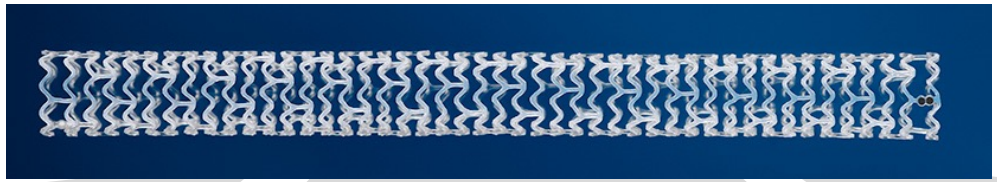
- Prospective, multicenter, single-blind, randomized controlled clinical study
- Approx. **225 patients** in up to **50 sites** in the US, Australia, New Zealand, Singapore and Taiwan
- Randomized in a 2:1 ratio (Esprit™ BTK:PTA)
- Subjects will be followed for **5 years**
- Study duration (expected)
  - First enrollment : Q3 2020
  - Enrollment Completion: Q1 2022



LIFE-BTK Trial



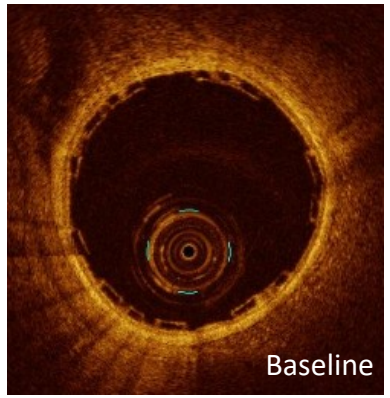
Esprit™ BTK Everolimus Eluting Resorbable Scaffold is a DRS under development for use in BTK disease

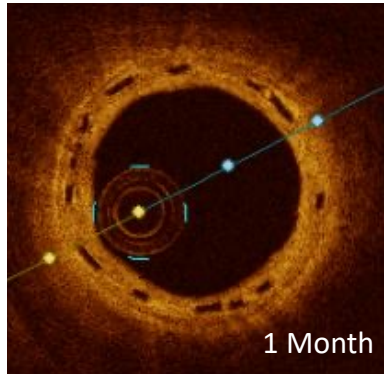


Everolimus	PDLLA Resorbable Coating	PLLA Resorbable Scaffold*
• 100 µg/cm^2 dose density	• Uniform drug delivery	• 99 µm strut thickness†
• Elution rate matched to restenosis cascade	• Provides sustained drug elution to maximize long term patency without downstream particulates	• Balloon expandable
• Cytostatic; broad therapeutic range		• Resists recoil; provides a platform for sustained drug delivery
		• Resorbs in a benign, controlled manner (~36 months)

*Platinum markers at proximal and distal ends remain for angiographic visualization
†≤ 3.0 mm size; 3.5 mm – 3.75 mm sizes have 120 µm strut thickness

PORCINE MODEL





Data and images on file at Abbott Vascular

CAUTION: Investigational device. Limited by Federal law to investigational use only.

Conclusion

- Although drug-enhanced therapy was successful in ATK, such success has not been realized for BTK disease.
- Ideal tibial treatment involves drug delivery, method of preventing recoil, but leaves future options open by leaving nothing behind
- Feasibility studies using first Gen Absorb everolimus-eluting resorbable scaffold demonstrated excellent long-term patency and freedom from TLR in tibial arteries while preserving future treatment options
- LIFE-BTK IDE study is well underway to assess the safety and efficacy of the Esprit BTK drug-eluting resorbable scaffold compared to PTA.

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