Bioresorbable Technology for BTK Arteries: Review of Existing Data and Future Trials

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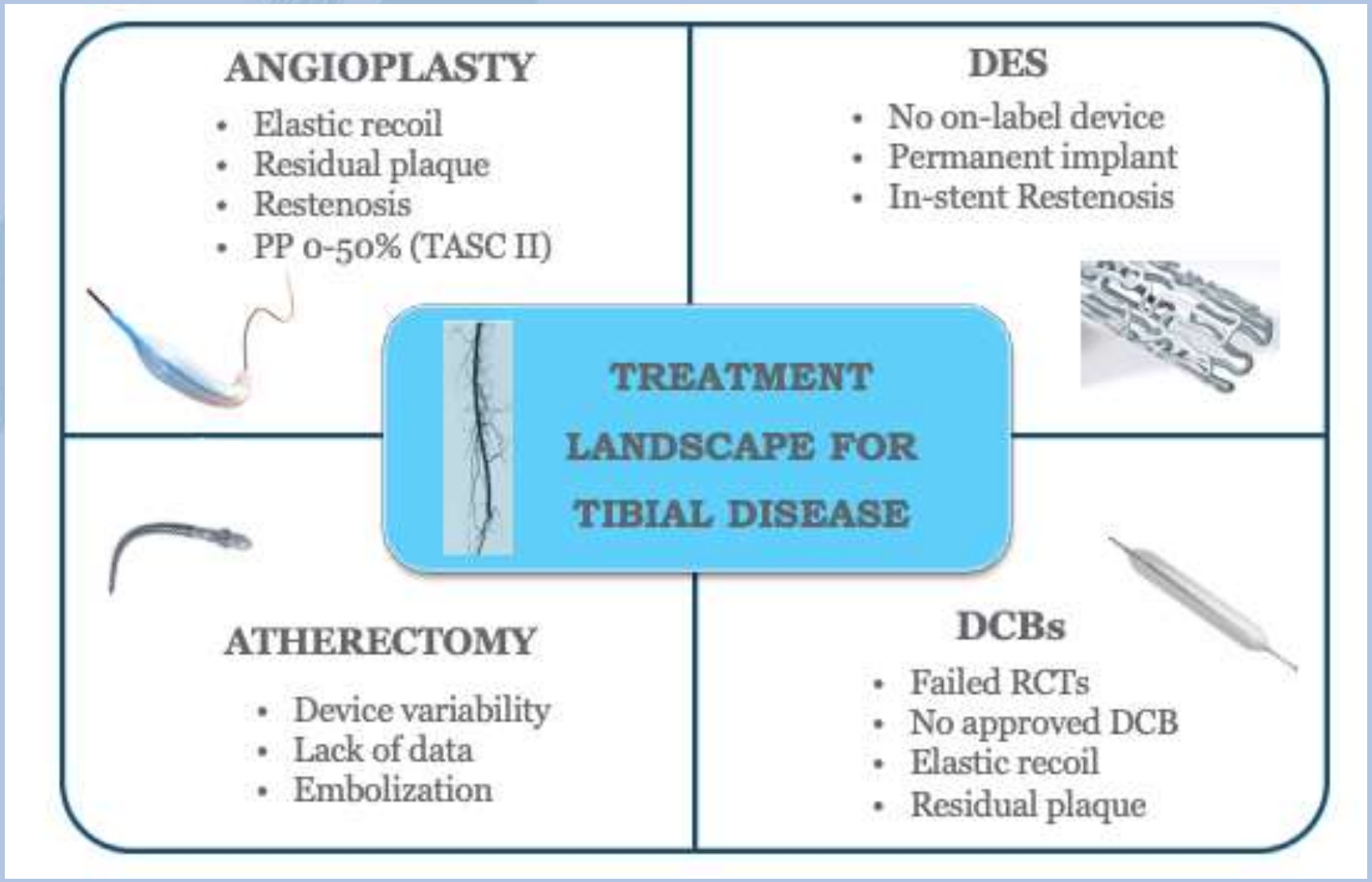
Disclosure Statement of Financial Interest

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

Company	Affiliation/Financial Relationship
• Abbott Vascular	• Scientific Advisory Board • Consulting agreement • Speakers fees / Honorarium
• Medtronic	• Scientific Advisory Board • Consulting agreement • Speakers fees / Honorarium • REALITY Trial National Co-PI
• Boston Scientific	• CLI Advisory Board
• BD / Bard	• Consulting agreement

BVS in the BTK Arteries – Existing Data & Future Trials



BVS in the BTK Arteries – Existing Data & Future Trials

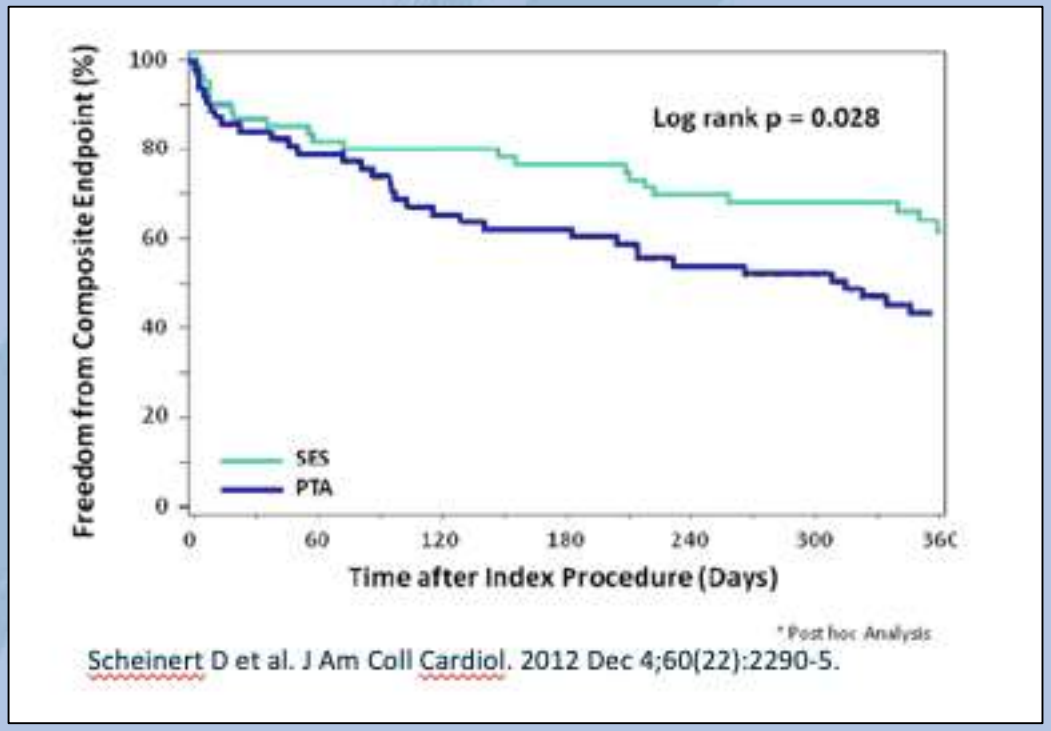
Randomized Controlled Trials of DES in Tibial Arteries

- DES shows benefit over BMS/PTA in multiple RCTs
- DES shows best patency results in BTK space and can address acute recoil / residual mechanical burden

- 12mo Primary Patency:

	DES	***BMS/PTA***
ACHILLES (vs PTA)	75%	57%
IDEAS (vs DCB PTA)	72%	42%
DESTINY (vs BMS)	85%	54%
YUKON-BTX (vs (BMS)	81%	56%

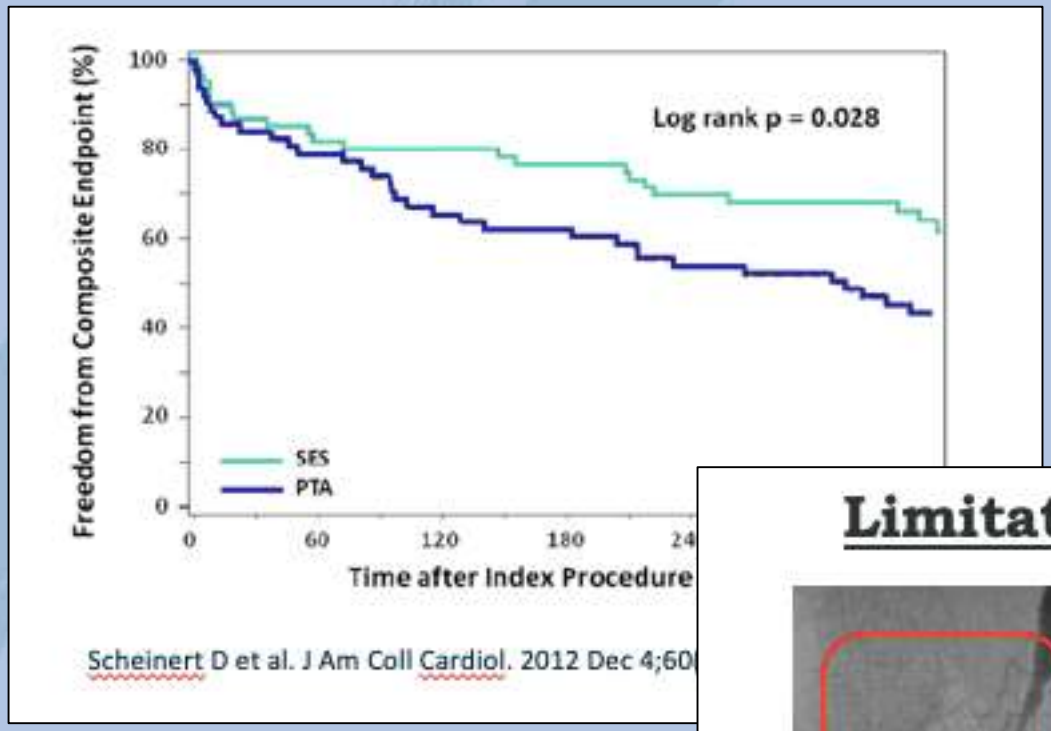
BVS in the BTK Arteries – Existing Data & Future Trials



Scheinert D et al. J Am Coll Cardiol. 2012 Dec 4;60(22):2290-5.

Metallic DES has shown superiority to DCB, BMS and PTA in RCTs

BVS in the BTK Arteries – Existing Data & Future Trials



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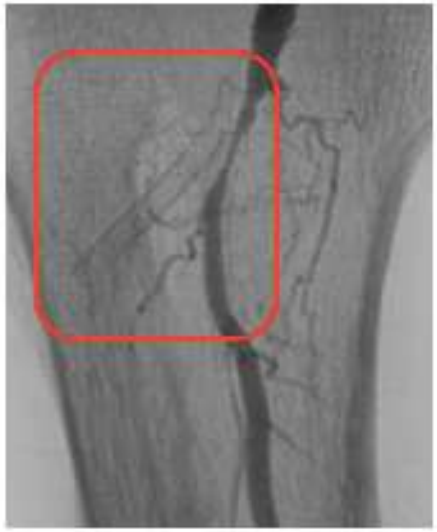
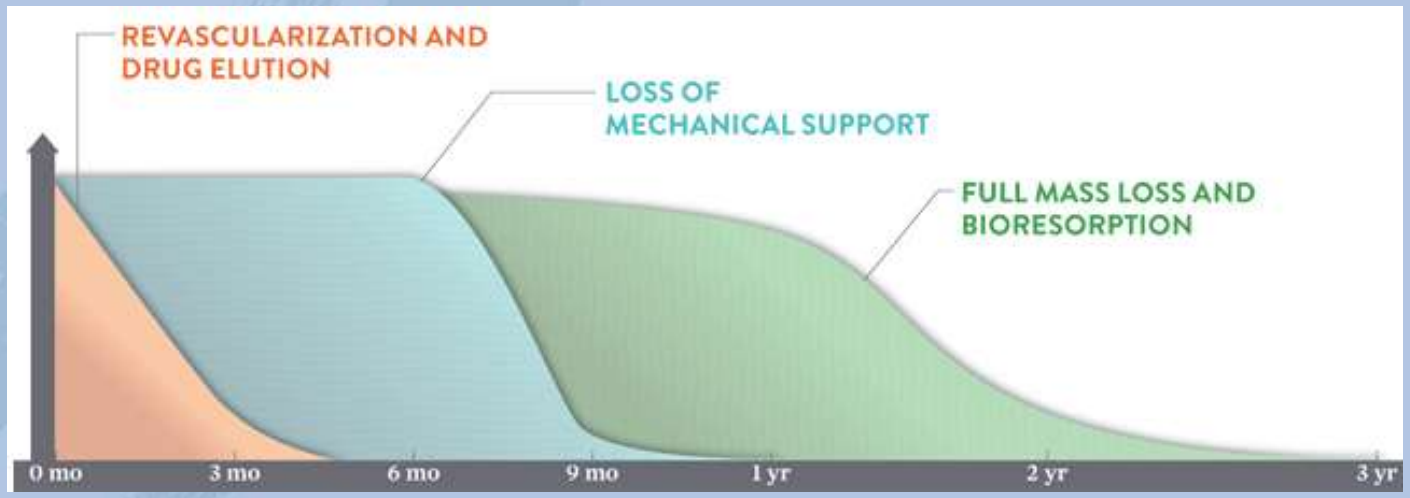
Metallic DES has shown superiority to DCB, BMS and PTA in RCTs

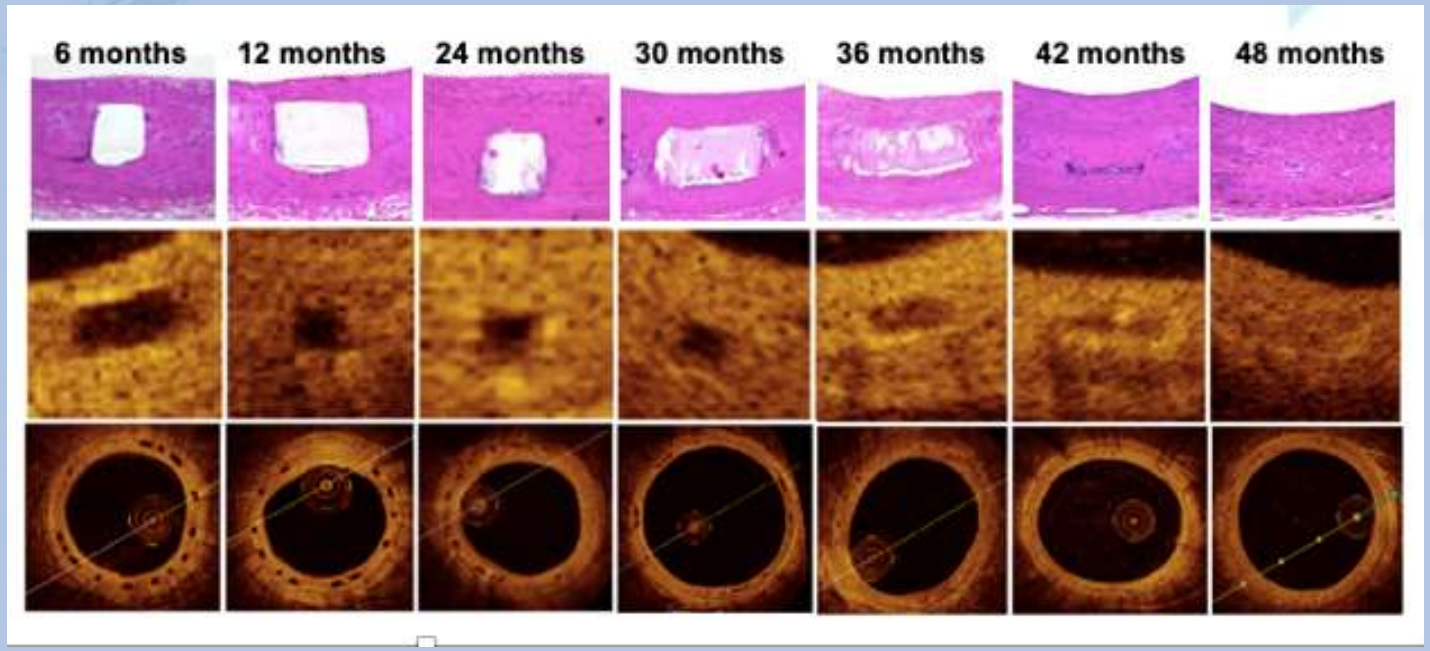
Limitations of Metallic DES:



- Off-label Use
- Short lengths
- Implications of permanent implant in CLI population

BVS in the BTK Arteries – Existing Data & Future Trials





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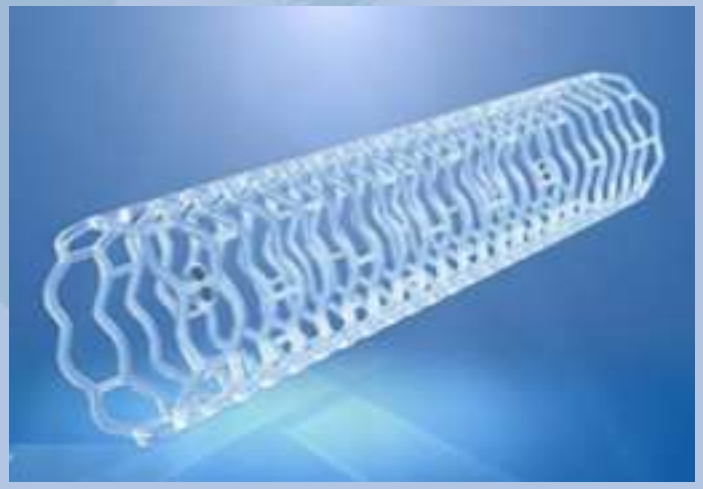


ABSORB GT1 BVS (Abbott)

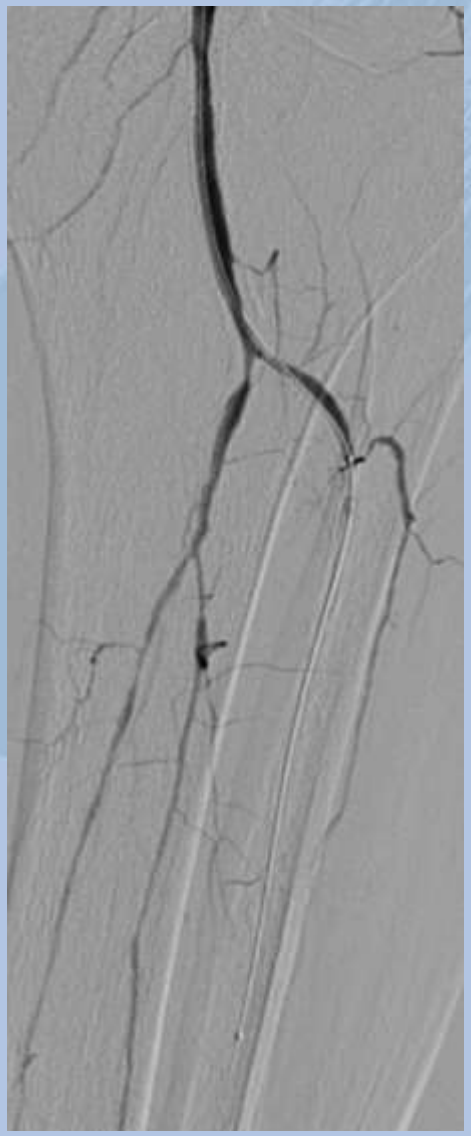
PLLA Scaffold

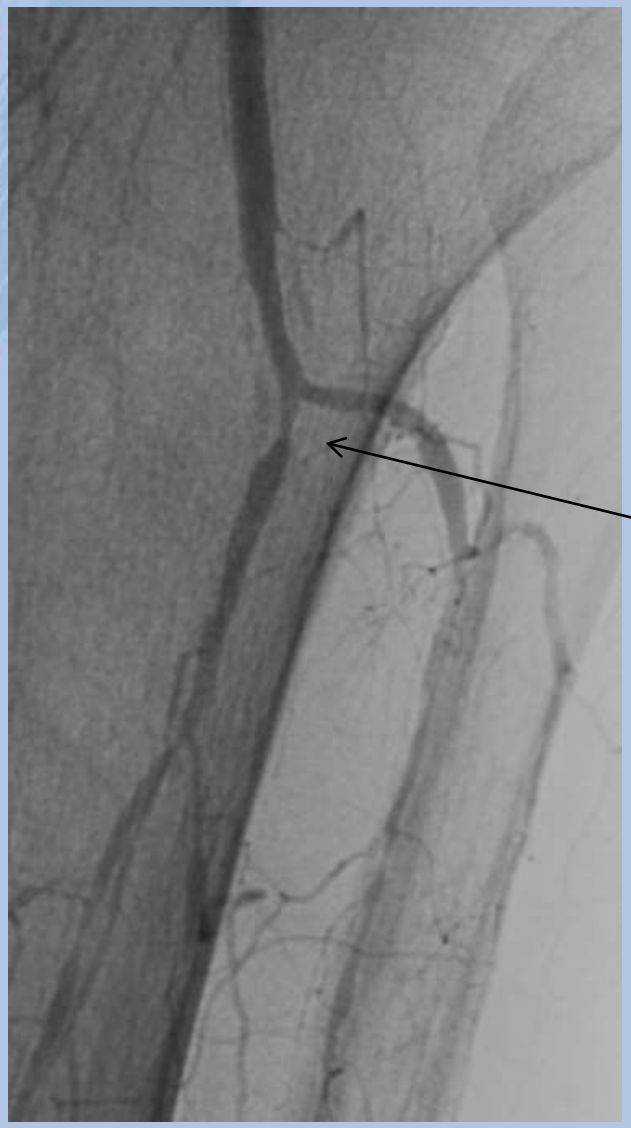
- Semi-crystalline poly-L-lactide backbone
- Provides device structure
- Developed to optimize radial strength

Everolimus / PDLLA Matrix Coating

- 2-4µm amorphous (non-crystalline) coating
- Poly-L,D-lactide matrix/Everlimus at 1:1 ratio
- Provides controlled drug release

BVS in the BTK Arteries – Existing Data & Future Trials

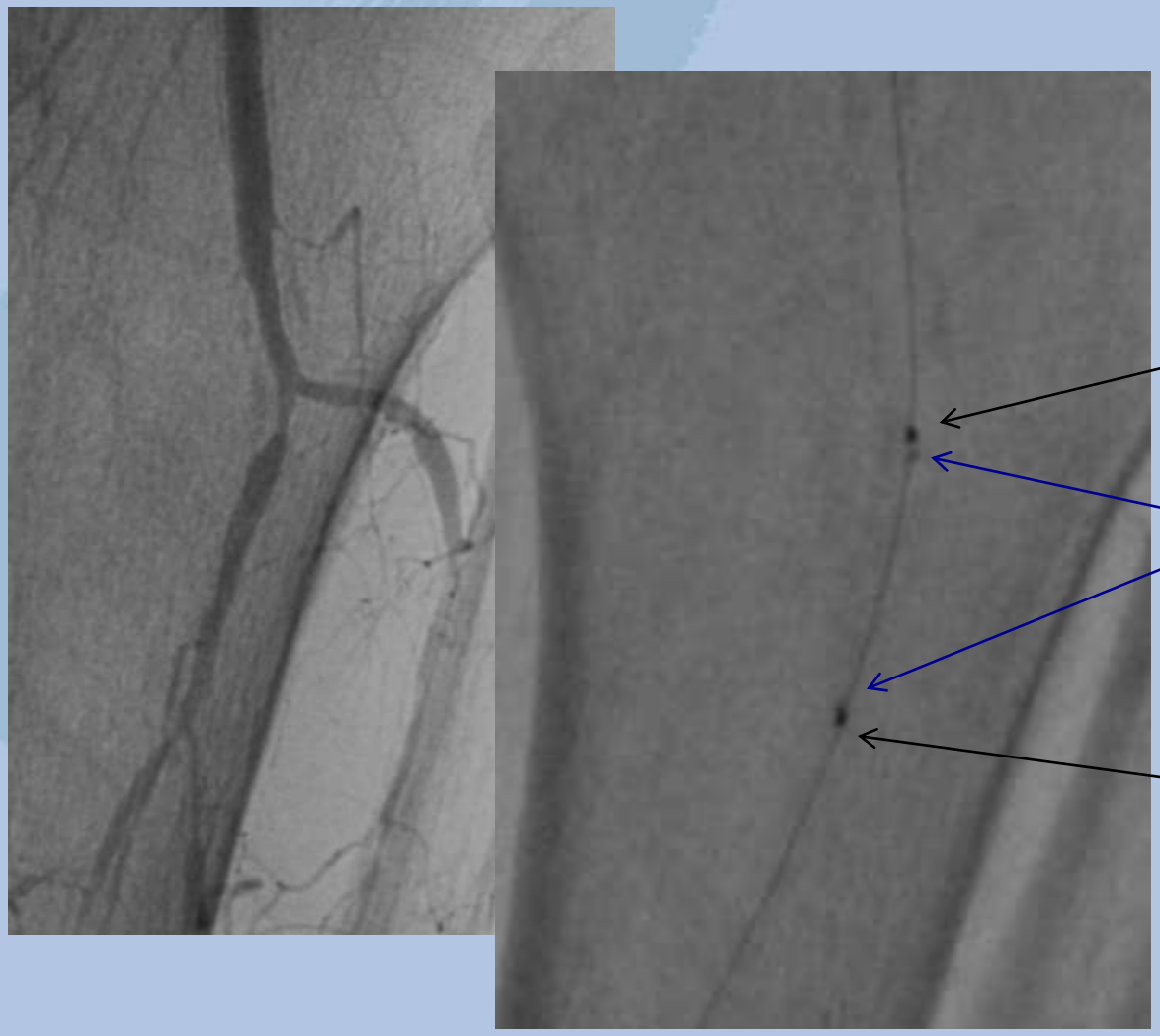




OCT for size assessment of reference vessel diameter

Focal predilatation with non-compliant 3.0x20 balloon

BVS in the BTK Arteries – Existing Data & Future Trials



3.0x28mm ABSORB GT1

Balloon marker

Platinum Scaffold markers

Balloon marker

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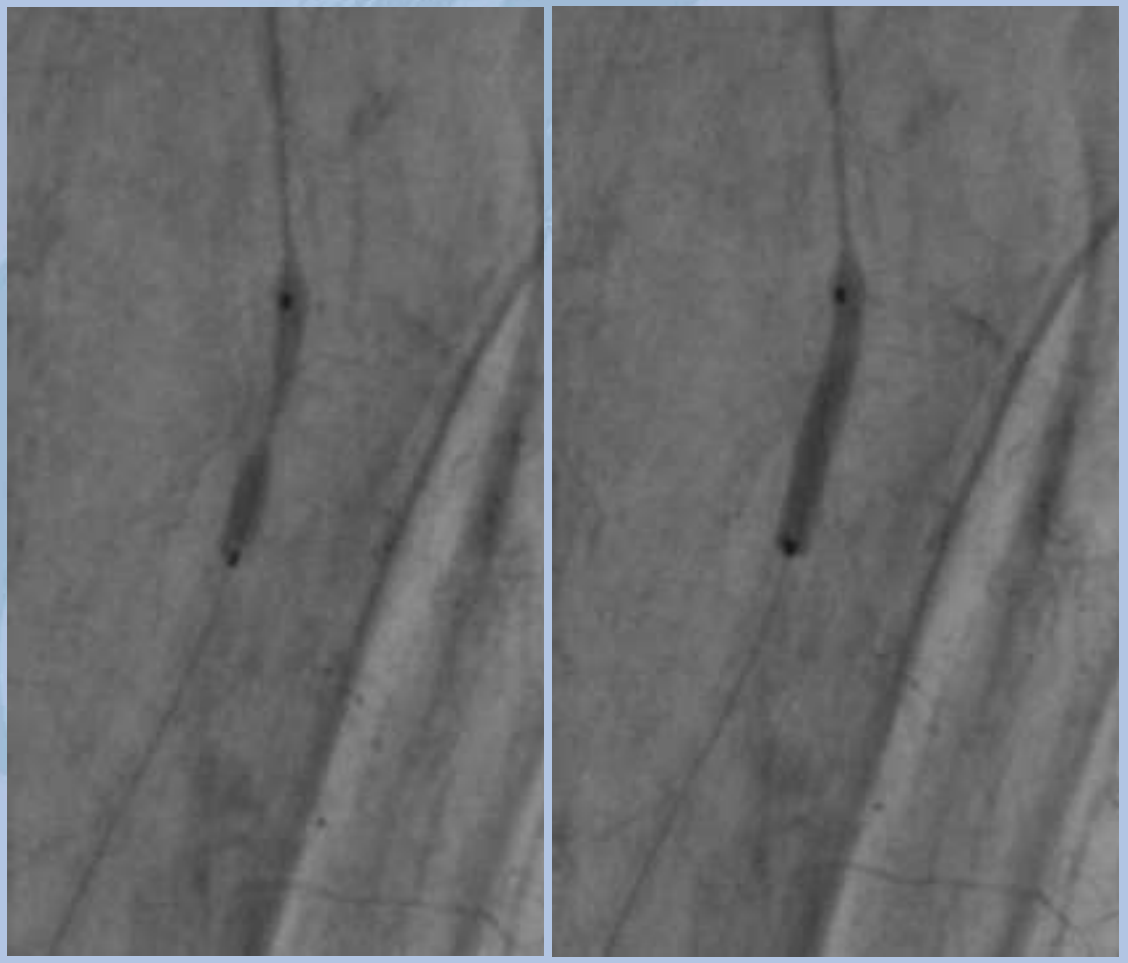
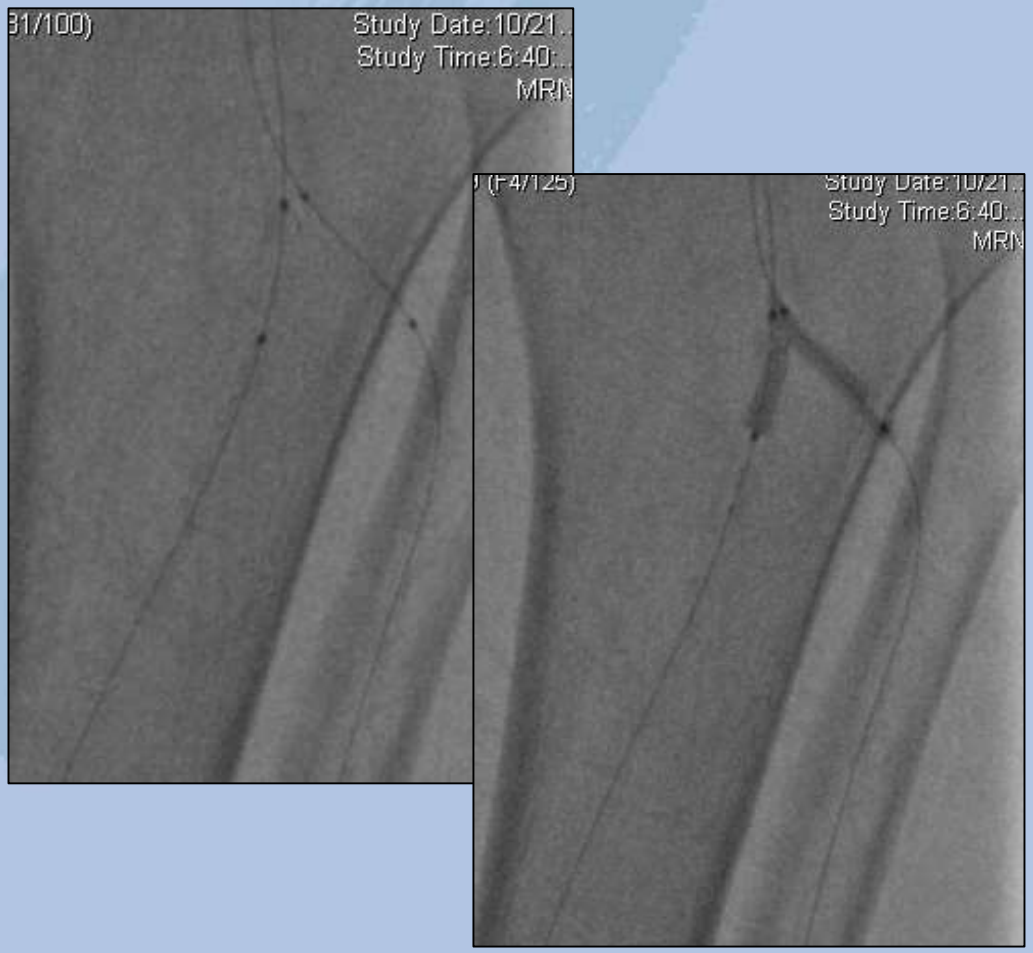
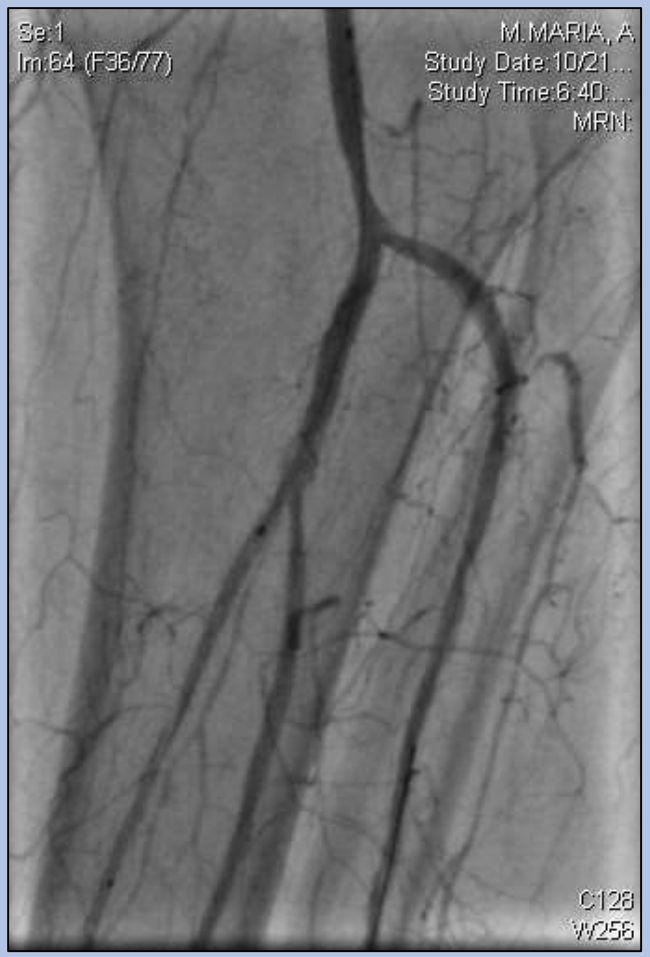


- Slow, controlled deployment to nominal diameter
- 2ATM increase every 5sec
- Post-dilate with 3.5x20 non-compliant balloon

BVS in the BTK Arteries – Existing Data & Future Trials





Brian G. DeRubertis, MD, FACS

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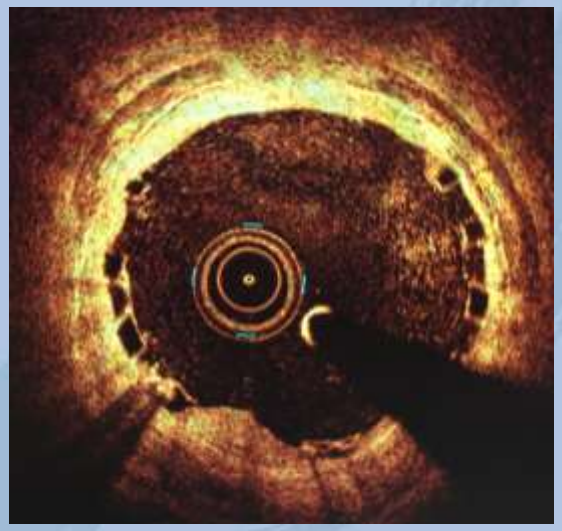

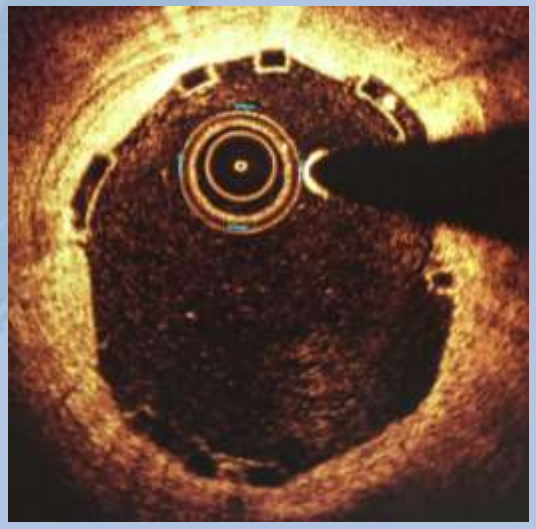

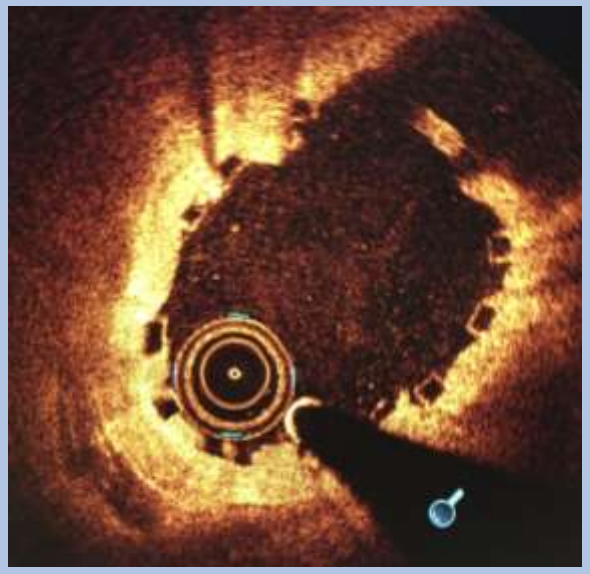

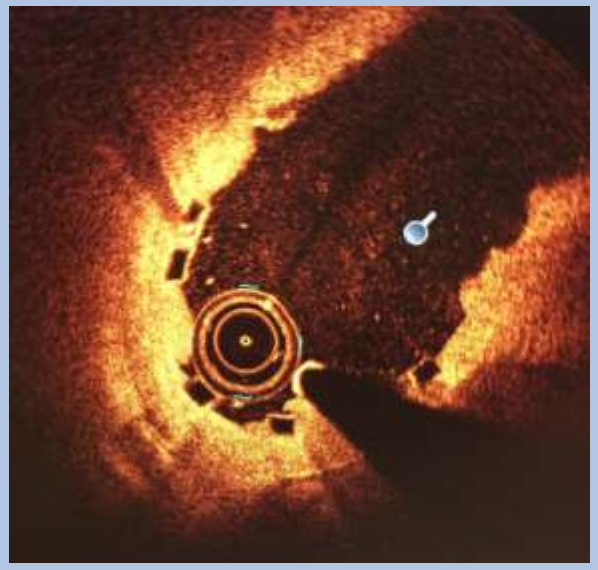

BVS in the BTK Arteries – Existing Data & Future Trials

Experience With the Absorb Everolimus-Eluting Bioresorbable Vascular Scaffold in Arteries Below the Knee

12-Month Clinical and Imaging Outcomes

Ramon L. Varcoe, MBBS, MS, PhD,[a,b,c] Olaf Schouten, MD, PhD,[a,d] Shannon D. Thomas, BSc Med Hons, MBBS,[a,b,c] Andrew F. Lennox, MBBS, MSc[a,c]

ABSTRACT

OBJECTIVES The aim of this study was to investigate the midterm performance of an everolimus-eluting, bioresorbable vascular scaffold (Absorb, Abbott Vascular, Santa Clara, California) for the treatment of focal tibial and distal popliteal lesions.

BACKGROUND Drug-eluting stents are used below the knee to improve technical success and durability, but the ongoing presence of a permanent metal scaffold may have deleterious effects on the local vessel.

METHODS Tibial and distal popliteal angioplasty with scaffold placement was performed using an everolimus-eluting, bioresorbable scaffold (Absorb). Clinical and ultrasound follow-up was performed at 1, 3, 6, 12, and 24 months to detect binary restenosis and evaluate safety, restenosis, and clinical improvement.

RESULTS Thirty-eight limbs in 33 patients were treated for critical limb ischemia (68.4%) or severe claudication (31.6%). Fifty scaffolds were used to treat a total of 43 lesions, with a mean length of 19.2 ± 11.6 mm. During a mean follow-up period of 12.0 ± 3.9 months, 5 patients died, and all others were available for follow-up. Among the 38 treated limbs, clinical improvement was present in 30 (79%). Binary restenosis was detected in 3 of 50 scaffolds (6%). Using the Kaplan-Meier method, rates of primary patency were 96% and 84.6% at 12 and 24 months, respectively, and rates of freedom from clinically driven target lesion revascularization were 96% and 96% at 12 and 24 months, respectively. Complete wound healing occurred in 64% of those treated for tissue loss, with no major amputation and a limb-salvage rate of 100%.

CONCLUSIONS Twelve-month follow-up demonstrated excellent safety, patency, and freedom from target lesion revascularization using the Absorb bioresorbable vascular scaffold below the knee. (J Am Coll Cardiol Intv 2016;9:1721-8) © 2016 by the American College of Cardiology Foundation.

Drug-eluting stents (DES) are effective for the treatment of Inter-Society Consensus for the Management of Peripheral Arterial Disease types A and B atherosclerotic arterial disease below the knee, reducing both abrupt closure and restenosis rates in the midterm (1–4). However, the metallic implant has several detrimental effects on the vessel, which include the permanent prevention of vasomotion, autoregulation, and adaptive remodeling. Moreover, there is a

From the [a]Department of Vascular Surgery, Prince of Wales Hospital, Sydney, Australia; [b]Faculty of Medicine, University of New

Varcoe, R. VIVA 2019

- 38 limbs in 33 patients
- 50 scaffolds implanted
- 43 infrageniculate lesions
- Mean lesion length 1.9cm
- 68% CLI, 32% Claudication

- Primary Patency (KM)
  - 12mo 96%
  - 24mo 85%

- Freedom from CD-TLR
  - 12mo 96%
  - 24mo 96%

BVS in the BTK Arteries – Existing Data & Future Trials

Experience With the Absorb Everolimus-Eluting Bioresorbable Vascular Scaffol

12-Month Clinical and In

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CONCLUSIONS Twelve-month follow-u
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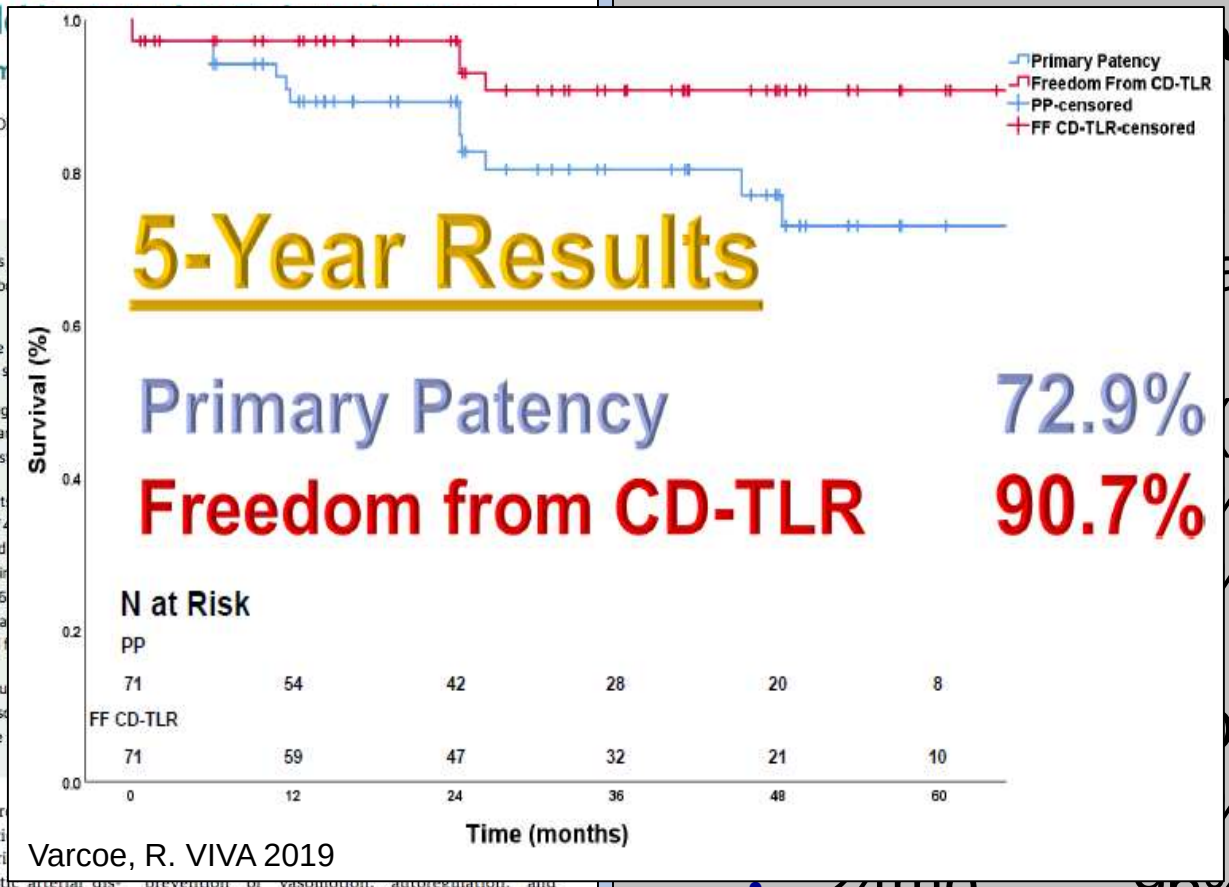

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  - lesions
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  - audication
  - (KM)
  - %
  - %
  - -TLR
  - %
  - 24mo 96%

BVS in the BTK Arteries – Existing Data & Future Trials

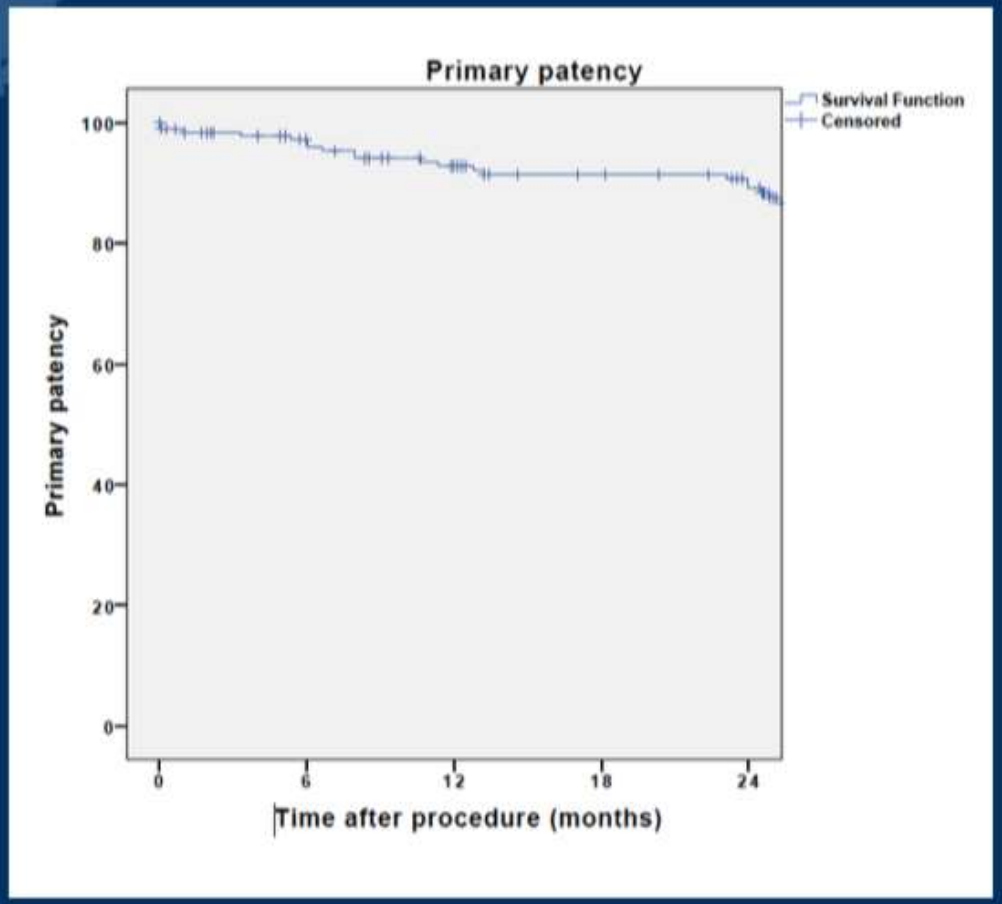
Pooled Analysis of Absorb Scaffolds in Tibial Arteries

- Consecutive patients treated with the Absorb BVS scaffold
  - Australia: Ramone Varcoe
  - Singapore: Steven Kum
  - USA: Atman Shaw
- August 2012 to May 2017
- Inclusion:
  - Rutherford 3-6
  - De novo BTK lesions distal popliteal or tibial arteries
  - Diameter between 2.5 to 4mm
- 189 scaffolds in 125 patients, mean length 26mm (4-88mm)

BVS in the BTK Arteries – Existing Data & Future Trials

Primary Patency
12 months 91.1%
24 months 88.6%

TLR
12 months 96.6%
24 months 94.5%



Varcoe, R. LINC 2020

BVS in the BTK Arteries – Existing Data & Future Trials

Landscape of Existing Devices Bioresorbable Devices

Scaffold	Company	Approval
ABSORB BVS	Abbott Vascular	FDA, CE
ESPRIT-BTK	Abbott Vascular	None
Magmaris	Biotronik	CE
MOTIV	Reva Medical	CE
Fantom	Reva Medical	CE
DESolve	Elixir Medical	CE
ART Scaffold	ART	CE

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BVS in the BTK Arteries – Existing Data & Future Trials

Future Trials: MOTIV Physician-Initiated Study

REVA

designs that disappear

REVA Enters Peripheral Artery Disease Space With First-Ever CE Mark of a Bioresorbale Scaffold for Below the Knee Therapy

July 25, 2018 | Source: REVA Medical Inc

SAN DIEGO, July 25, 2018 (GLOBE NEWSWIRE) -- REVA Medical, Inc. (ASX:RVA) ("REVA" or the "Company"), a leader in bioresorbable polymer technologies for vascular applications, today announced that its MOTIV™ bioresorbable scaffold is the first drug-eluting bioresorbable scaffold to receive CE Mark approval for treatment of below the knee peripheral artery disease. Late last year, REVA announced its plans to expand use of its bioresorbable scaffold technology in peripheral artery disease. The approval of MOTIV delivers that milestone and for the first time brings bioresorbable technology to this patient population.

MOTIV is made from Tyrocore, REVA's proprietary polymer designed specifically for vascular scaffolds. Tyrocore is inherently radiopaque, making MOTIV visible under x-ray to ensure accurate placement in the artery. The Company will identify over the next few months select centers to assess the product's performance, inform future product development activities and determine its complete commercial strategy in peripheral vascular applications. REVA expects MOTIV's first use in patients to be in late 2018 or early next year.

- Tyrocore (Iodinated Diphenol) scaffold
- Sirolimus @ 1.97ng/mm
- 2.5mm, 3.0mm, and 3.5mm diameters (expansion up to 4.0mm)
- 12mm, 18mm, 24mm lengths

BVS in the BTK Arteries – Existing Data & Future Trials

Future Trials: MOTIV Physician-Initiated Study


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designs that disappear

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SAN DIEGO, July 25,

- Prospective, single arm, single-center study
- Total of 15 patients
- Follow up period of 12 months
- Rutherford 4-5
- De novo or restenotic lesions
- Target vessel diameter of 2.5-3.5mm
- Total lesion length <40mm

BVS in the BTK Arteries – Existing Data & Future Trials

Future Trials: ESPRIT-BTK (Abbott Vascular)

ESPRIT-BTK

PLLA SCAFFOLD

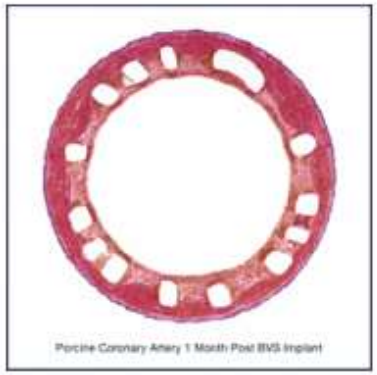
- Fully resorbable*
- Platinum markers for angiographic visualization
- 99 µm strut thickness†
- Supports treated artery
- Allows for uniform delivery of everolimus
- Resorbs in a benign, controlled manner (~36 mo).

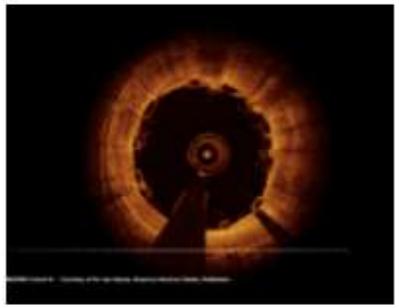
PDLLA COATING

- Fully resorbable
- Conformal coating
- 1:1 PDLLA: everolimus blend
- Provides sustained everolimus release to maximize long term patency without downstream particulates

EVEROLIMUS

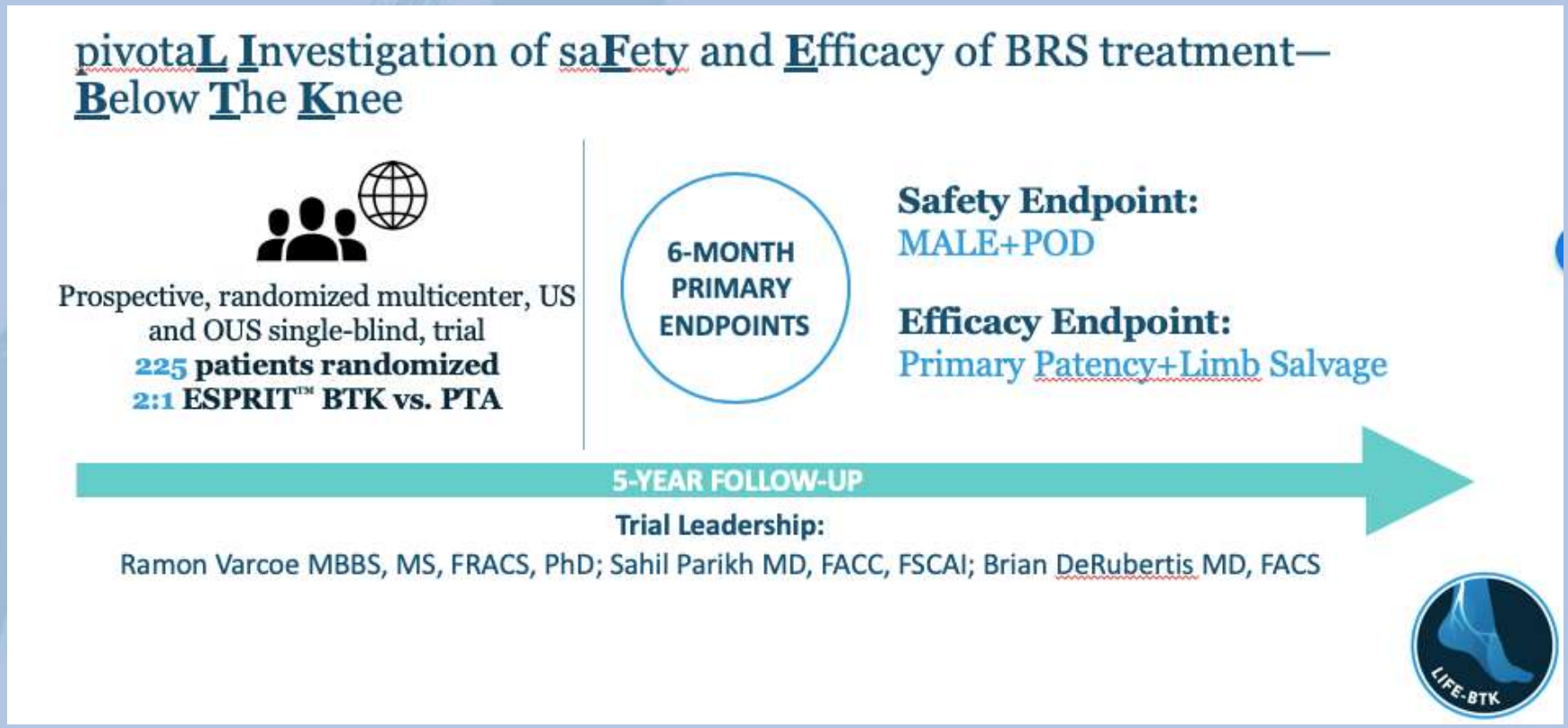
- Cytostatic
- Patented for restenosis reduction
- Broad therapeutic range
- 100 µg/cm² dose density
- Elution rate matched to restenosis cascade





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

BVS in the BTK Arteries – Existing Data & Future Trials



- Rutherford 4-5
- De novo or restenotic infrapopliteal lesions
- Maximum lesion length 100mm
- Up to 3 scaffolds in target lesion
- Reference vessel diameter 2.5-3.5mm

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