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.

<table>
<thead>
<tr>
<th>Company</th>
<th>Affiliation/Financial Relationship</th>
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<tbody>
<tr>
<td>Abbott Vascular</td>
<td>• Scientific Advisory Board&lt;br&gt;• Consulting agreement&lt;br&gt;• Speakers fees / Honorarium</td>
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<tr>
<td>Medtronic</td>
<td>• Scientific Advisory Board&lt;br&gt;• Consulting agreement&lt;br&gt;• Speakers fees / Honorarium&lt;br&gt;• REALITY Trial National Co-PI</td>
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<tr>
<td>Boston Scientific</td>
<td>• CLI Advisory Board</td>
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<tr>
<td>BD / Bard</td>
<td>• Consulting agreement</td>
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</table>
BVS in the BTK Arteries – Existing Data & Future Trials

ANGIOPLASTY
- Elastic recoil
- Residual plaque
- Restenosis
- PP 0-50% (TASC II)

DES
- No on-label device
- Permanent implant
- In-stent Restenosis

TREATMENT LANDSCAPE FOR TIBIAL DISEASE

ATHERECTOMY
- Device variability
- Lack of data
- Embolization

DCBs
- Failed RCTs
- No approved DCB
- Elastic recoil
- Residual plaque
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:

<table>
<thead>
<tr>
<th>Trial</th>
<th>DES</th>
<th>BMS/PTA</th>
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<tbody>
<tr>
<td>ACHILLES (vs PTA)</td>
<td>75%</td>
<td>57%</td>
</tr>
<tr>
<td>IDEAS (vs DCB PTA)</td>
<td>72%</td>
<td>42%</td>
</tr>
<tr>
<td>DESTINY (vs BMS)</td>
<td>85%</td>
<td>54%</td>
</tr>
<tr>
<td>YUKON-BTX (vs (BMS)</td>
<td>81%</td>
<td>56%</td>
</tr>
</tbody>
</table>
Metallic DES has shown superiority to DCB, BMS and PTA in RCTs
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


Log rank p = 0.028
BVS in the BTK Arteries – Existing Data & Future Trials

Loss of mechanical support and full mass loss and biodegradation over time.
BVS in the BTK Arteries – Existing Data & Future Trials

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
Focal predilatation with non-compliant 3.0x20 balloon

OCT for size assessment of reference vessel diameter

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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
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BVS in the BTK Arteries – Existing Data & Future Trials

Brian G. DeRubertis, MD, FACS
Experience With the Absorb Everolimus-Eluting Biodegradable Vascular Scaffold in Arteries Below the Knee
12-Month Clinical and Imaging Outcomes

Ramon L. Varcoe, MBBS, MS, PhD, a, b Olaf Schouten, MD, PhD, a, c Shannon D. Thomas, BSc Med Hon, MBBS, a, b, c Andrew F. Lecom, MBBS, MS, d

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 ± 6.4 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 95% at 12 and 24 months, respectively. Complete wound healing occurred in 96% 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. (*Am Coll Cardiol Intv 2016;9:1271-8) © 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 Artery 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, including the following: which include the permanent prevention of vasomotion, autoregulation, and adaptive remodeling. Moreover, there is a

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

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

Varcoe, R. VIVA 2019
Experience With the Absorb Everolimus-Eluting Bioresorbable Vascular Scaffold

12-Month Clinical and Intermediate Follow-Up

Ramón L. Varcoe, MBBS, MS, PhD
Andrew F. Leemans, MBBS, MS

ABSTRACT

OBJECTIVES The aim of this study was to assess the safety and effectiveness of the bioresorbable vascular scaffold (Absorb, Abbott) for the treatment of infrageniculate lesions.

BACKGROUND Drug-eluting stents are the standard of care for the treatment of de novo, restenotic, and in-stent restenotic lesions. The primary objective of the current study is to evaluate the safety and effectiveness of the Absorb scaffold for the treatment of infrageniculate lesions.

METHODS A prospective, multicenter, single-arm, open-label study was performed in 33 patients. The Absorb scaffold was implanted in 38 limbs of 33 patients with infrageniculate lesions. The mean lesion length was 1.9 cm, with 68% CLI and 32% claudication.

RESULTS Thirty-eight limbs in 33 patients were enrolled. Fifty scaffolds were implanted in 38 limbs of 33 patients. Angiographic follow-up was performed at 6 months. The primary patency rate at 12 months was 96%, and at 24 months, it was 85%. Freedom from CD-TLR was 96% at both 12 and 24 months. The freedom from target lesion revascularization (TLR) was 96% at both 12 and 24 months.

CONCLUSIONS The Absorb scaffold is safe and effective for the treatment of infrageniculate lesions. The primary patency and freedom from CD-TLR rates are comparable to those of drug-eluting stents.

Varcoe, R. VIVA 2019

5-Year Results

Primary Patency  72.9%
Freedom from CD-TLR  90.7%

BVS in the BTK Arteries – Existing Data & Future Trials

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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
Landscape of Existing Devices Bioresorbable Devices

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<td>Abbott Vascular</td>
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# BVS in the BTK Arteries – Existing Data & Future Trials

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Future Trials: MOTIV Physician-Initiated Study

- 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
Future Trials: MOTIV Physician-Initiated Study

- 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
Future Trials: ESPRIT-BTK (Abbott Vascular)

- **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

**Pivotal Investigation of Safety and Efficacy of BRS treatment—Below The Knee**

- 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 Parikh MD, FACC, FSCAI
  - Brian DeRubertis MD, FACS

- 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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