Are the Coronary Outcomes of BVS Relevant to BTK Applications?

LINC 2018
January 30 – February 2, 2018
Leipzig, Germany

Brian DeRubertis, MD, FACS
Associate Professor of Surgery
UCLA Division of Vascular Surgery
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>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott Vascular</td>
<td>Scientific Advisory Board</td>
</tr>
<tr>
<td></td>
<td>Consulting agreement</td>
</tr>
<tr>
<td></td>
<td>Speakers fees / Honorarium</td>
</tr>
<tr>
<td>Medtronic</td>
<td>Scientific Advisory Board</td>
</tr>
<tr>
<td></td>
<td>Consulting agreement</td>
</tr>
<tr>
<td></td>
<td>Speakers fees / Honorarium</td>
</tr>
<tr>
<td></td>
<td>REALITY Trial National Co-PI</td>
</tr>
<tr>
<td>Boston Scientific</td>
<td>CLI Advisory Board</td>
</tr>
<tr>
<td>Cook Medical</td>
<td>Proctoring and Case Review</td>
</tr>
<tr>
<td></td>
<td>Honorarium</td>
</tr>
</tbody>
</table>
Are the Coronary Outcomes of BVS Relevant to BTK?

- Is there a clinical need for BVS below the knee?
- Is there a commercial market for BVS in the periphery?
- Are there lessons from the coronary circulation that may be relevant to the below knee space?
- Do failures of coronary BVS mean we should curb our enthusiasm for this technology BTK?
Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a clinical need for BVS below the knee?

### Treatment Options for the Tibial Circulation:

**Angioplasty**
- Elastic recoil
- Residual plaque
- Restenosis
- 20-50% PP (TASC II)

**Atherectomy**
- Device variability
- Lack of data
- Embolization

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

**DES**
- No on-label device
- Permanent implant
- Short lengths
Are the Coronary Outcomes of BVS Relevant to BTK?

*Is there a clinical need for BVS below the knee?*

- 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></th>
<th><strong>DES</strong></th>
<th><strong>BMS/PTA</strong></th>
</tr>
</thead>
<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>
Are the Coronary Outcomes of BVS Relevant to BTK?

**Is there a clinical need for BVS below the knee?**

- **Limitations of DES:**
  - Off-label use
  - Short lengths
  - Implications of permanent impact in CLI population

**Simple answer:**
Yes! We need better therapies for the below knee space as we continue to utilize balloon angioplasty as the mainstay of treatment for tibial lesions
Are the Coronary Outcomes of BVS Relevant to BTK?

**Is there a clinical need for BVS below the knee?**

**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
Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a clinical need for BVS below the knee?

Day 1 6 mo 2 yr 5 yr

Courtesy of RJ van Geuns, Erasmus Medical Center, Netherlands
Are the Coronary Outcomes of BVS Relevant to BTK?

*Is there a clinical need for BVS below the knee?*

- OCT for size assessment of reference vessel diameter
- Focal predilatation with non-compliant 3.0x20 balloon
Are the Coronary Outcomes of BVS Relevant to BTK?

*Is there a clinical need for BVS below the knee?*
Are the Coronary Outcomes of BVS Relevant to BTK?

**Is there a clinical need for BVS below the knee?**

- Slow, controlled deployment to nominal diameter
- 2ATM increase every 5sec
- Post-dilate with 3.5x20 non-compliant balloon
Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a clinical need for BVS below the knee?
Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a clinical need for BVS below the knee?
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,c Olf Schouten, MD, PhD, a,c Shannon D. Thomas, BSc Med Hon, MBBS,a,b,c Andrew F. Lermox, MBBS, MS,c,a,b,c

ABSTRACT

OBJECTIVES The aim of this study was to investigate the midterm performance of an everolimus-eluting, biodegradable 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, biodegradable 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 biodegradable 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 wall, which include the permanent prevention of vasomotion, autoregulation, and adaptive remodeling. Moreover, there is a

Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a clinical need for BVS below the knee?

- 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%

From the Department of Vascular Surgery, Prince of Wales Hospital, Sydney, Australia. Faculty of Medicine, University of New
Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a commercial market for BVS in the periphery?

<table>
<thead>
<tr>
<th>Scaffold</th>
<th>Company</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSORB BVS</td>
<td>Abbott Vascular</td>
<td>FDA, CE</td>
</tr>
<tr>
<td>Magmaris</td>
<td>Biotronik</td>
<td>CE</td>
</tr>
<tr>
<td>Fantom</td>
<td>Reva Medical</td>
<td>CE</td>
</tr>
<tr>
<td>DESolve</td>
<td>Elixir Medical</td>
<td>CE</td>
</tr>
<tr>
<td>ART Scaffold</td>
<td>ART</td>
<td>CE</td>
</tr>
</tbody>
</table>

- All approved devices approved are for and marketed toward coronary circulation, following on the success of DES
- PCI market: ~$2.5 billion in U.S. (declining)

Problem for BVS in Coronary circulation:

**DES sets extremely high bar for improvement!!!**
Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a commercial market for BVS in the periphery?

**NEWS • INTERVENTIONAL • ACC 2017**

**ABSORB III: Two-Year Results Show a Higher Compared With Xience**

Although the FDA today issued a letter informing doctors of risks with investigators believe the 2-year data are actually reassuring.

**NEWS • TCT 2016**

‘Worrisome’ 3-Year Data From ABSORB II Raise Concerns About First-Generation Bioresorbable Stent

By Michael O’Riordan | October 30, 2016

---

**Late (2-3-year) difference in:**
- Target lesion failure
- Stent thrombosis

**No differences in:**
- Cardiac death
- All-cause death
- Patient-oriented cardiovascular events

---

**WASHINGTON, DC—**Three-year outcomes from the ABSORB II trial, a time point in which the Absorb GT1 bioresorbable vascular scaffold should be degraded, did not result in an improvement in vasomotor tone and was associated with an increase in late lumen loss when compared with the Xience everolimus-eluting metallic stent.

The study also showed that treatment with Absorb (Abbott Vascular) was associated with a two-fold increased risk of device-oriented clinical events, specifically an increased risk of target-vessel revascularization. The ratio of device-oriented clinical events between the Absorb and Xience groups was 1.95 (95% CI 1.23–3.06) at 3 years.
Are the Coronary Outcomes of BVS Relevant to BTK?

Is there a commercial market for BVS in the periphery?

Difference between the coronaries and the periphery:

- No “high bar” in periphery
- Scaffold with anti-restenosis effect and lack of negative implications (i.e., permanent implant) could have wildly significant levels of adoption
- Global commercial market for PCI is similar to PAD, but decreasing, while the global cost of PAD is staggeringly high
- At least 30% of patients with CLI who undergo amputation do so without revascularization.
- This implies that the market for new CLI therapies will increase as access to appropriate care increases
Are the Coronary Outcomes of BVS Relevant to BTK?

Are there lessons to be learned from the coronary circulation?

• Patency \( \downarrow \) with scaffold diameters <2.25mm
  - Size, and potential for mechanical/compressive forces make BVS unlikely to do well in pedal vessels
• Proper technique is essential to good outcomes
  - Pre-dilatation
  - appropriate Sizing
  - Post-dilatation
  - Adjunctive imaging
Are the Coronary Outcomes of BVS Relevant to BTK?

**PSP** *(Pre-dilate, appropriate Sizing, Post-dilation)*
Are the Coronary Outcomes of BVS Relevant to BTK?

**PSP (Pre-dilate, appropriate Sizing, Post-dilation)**
Are the Coronary Outcomes of BVS Relevant to BTK?

Should failures in the coronary circulation deter us from pursuing BVS for the BTK space?

- Answer is overwhelmingly "NO!!!"

- Caution:
  - Pay attention to lessons learned
    - Strut thickness
    - Technique
    - Scaffold sizing
  - Continue to pursue next-generation improvements
Are the Coronary Outcomes of BVS Relevant to BTK?

**Should failures in the coronary circulation deter us from pursuing BVS for the BTK space?**

- Answer is overwhelmingly “NO!!!”
- **Enthusiasm:**
  - Is a 2-3% difference in late scaffold thrombosis relevant to patient with 50% 5-year mortality and 30-50% likelihood of restenosis with current standard of care?
  - Our industry colleagues need to uncouple the success with BTK BVS from coronary success or our patients may suffer from a tremendous missed opportunity for improved outcomes
Are the Coronary Outcomes of BVS Relevant to BTK Applications?

LINC 2018
January 30 – February 2, 2018
Leipzig, Germany

Brian DeRubertis, MD, FACS
Associate Professor of Surgery
UCLA Division of Vascular Surgery