Perspective in Interventional Cardiology: The Bioresorbable Stent

A Revolutionary Advance in Percutaneous Revascularization

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Centennial Heart & Cardiovascular
Above all else, guard your heart for it is the wellspring of life
Proverbs 4:23
The current acceptable origin of the word *stent* is that it derives from the name of a dentist. Charles Thomas Stent (1807 to 1885) was an English dentist.

Percutaneous Interventional Cardiology has revolutionized the way we treat ischemic heart disease... but the 5th revolution is on the horizon...
The Way Things Used to Be….

1977 — **Andreas Gruentzig** performed first cath lab PTCA on awake patient in Zurich; starting with this case, all PTCA data is entered into a worldwide registry.

**Directional Coronary Atherectomy**

1982: Bare Metal Stent: Julio Palmaz & Richard Schatz: stainless steel stent for coronary applications.


2002: Drug-eluting stents introduces

**Bioresorbable drug-eluting stents**
The Way Things Are Now....
At least in Europe

Fully Bioreosorbable
Hypothesis:
1. Vascular scaffolding is a temporary need
2. Improved long term outcomes with temporary scaffolding to bridge healing phase post PTCI
Potential Benefits of Bioresorbable Scaffolds over Standard DES

- Absence of Permanent Rigid Metallic Cage
- Restoration of vasomotion
- Late luminal enlargement
- Preservation of targets for CABG
- Appeal to physician/patient
- Freedom from long-term polymer exposure
- Angina relief
- Side branch “jailing”
- Artifacts with non-invasive imaging: CTA

CRITICAL ELEMENT

Is there evidence these “potentials” will improve patient outcomes?
The Three Steps of The Stent Life Cycle

Revascularization

Restoration

Resorption
Lifecycle of a Biodegradable Scaffold

- Drug elution to reduce risk of restenosis
  - Media healing post disruption
- Mechanical support to maintain patency
  - PTCA causes media disruption and a dissection

REVASCULARIZATION

Scaffold Mass

Drug Elution

Scaffold Support

0 3 6 Months
Lifecycle of a Bioresorbable Scaffold

- Drug elution complete
- Mechanical support to maintain patency
Lifecycle of a Bioresorbable Scaffold

- Polymer exposure complete
- Scaffold support no longer required
- Natural vasomotion and positive remodeling enabled
<table>
<thead>
<tr>
<th>Company</th>
<th>Stent</th>
<th>FHU</th>
<th>CE Mark</th>
<th>IDE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reva</td>
<td>ReZolve</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ART</td>
<td>Pure BRS</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Abbott</td>
<td>Absorb BVS</td>
<td>✓</td>
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<tr>
<td>Amaranth</td>
<td>Fortitude</td>
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<td>Elixir</td>
<td>DESolve</td>
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<tr>
<td>Reva</td>
<td>Fantom</td>
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<td>Biotronik</td>
<td>DREAMS 2</td>
<td>✓</td>
<td>☀</td>
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<tr>
<td>Amaranth</td>
<td>Aptitude</td>
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<tr>
<td>Elixir</td>
<td>DESolve Cx</td>
<td>☀</td>
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<td>✓</td>
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<tr>
<td>BSC</td>
<td>FAST</td>
<td>☀</td>
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</table>

- ✓ Complete
- ☀ Initiated
Absorb BVS

**Everolimus/PDLLA (1:1) matrix coating**
- 7 µm
- Conformal coating
- Controlled drug release similar to Xience CoCr-EES

**PLLA Backbone**
- Semi-crystalline
- Circumferential sinusoidal rings connected by linear links
- Strut thickness 150 µm
- Platinum markers in each end ring
Abbott Vascular Everolimus-Eluting Bioresorbable Vascular Scaffold Components

**Bioresorbable Scaffold**
- Poly (L-lactide) (PLLA)
- Based on proven MULTI-LINK pattern
- Naturally resorbed, fully metabolized

**Bioresorbable Coating**
- Poly (D,L-lactide) (PDLLA)
- Naturally resorbed, fully metabolized

**Everolimus**
- Similar dose density and release rate to XIENCE V

**XIENCE V Delivery System**
- World-class deliverability
Current Generation BRS – Ready for Prime Time?

Benefits

Limitations / Potential Risks

Current Generation Bioresorbable Scaffolds
Clinical Data and the Bioresorbable Stent Platform
Absorb III Program Objectives
A Series of Randomized Trials Designed to:

• Demonstrate similar (non-inferior) results with ABSORB BVS compared to Xience CoCr-EES at 1 year

• Demonstrate superior results with ABSORB BVS compared to Xience CoCr-EES between 1 and 5 years
ABSORB III Study Design

Prospective, multicenter, single-blind, trial
~2,000 patients randomized
2:1 Absorb BVS vs. Xience CoCr-EES

Clinical follow-up:

30 d  6 mo  12 mo  24 mo  36 mo  48 mo  60 mo

No routine angiographic follow-up
Not powered for clinical event rates
Primary Endpoint: Target Lesion Failure (non-inferiority)

- Cardiac death, or
- Myocardial infarction attributed to the target vessel (TV-MI), or
  - Peri-procedural MI: CK-MB >5x ULN w/i 48 hours
- Ischemia-driven target lesion revascularization (ID-TLR)

Powered Secondary Endpoints (superiority)

- Angina
- All revascularization
- Ischemia-driven target vessel revascularization (ID-TVR)
Study Flow and Follow-up

Randomized 2:1
N=2008 (ITT)

ABSORB
N=1322
N=4 lost to follow-up
N=6 withdrew consent

99.2% Complete

12-month Follow-up

Xience
N=686
N=6 lost to follow-up
N=3 withdrew consent

98.7% Complete
## Acute Success

<table>
<thead>
<tr>
<th></th>
<th>Absorb (N=1322, L=1385)</th>
<th>Xience (N=686, L=713)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Device Success</strong></td>
<td>94.3%</td>
<td>99.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Procedural Success</strong></td>
<td>94.6%</td>
<td>96.2%</td>
<td>0.12</td>
</tr>
</tbody>
</table>

### Device Success (lesion basis)
- Successful delivery and deployment of study scaffold/stent at intended target lesion
- Successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA)

### Procedure Success (patient basis)
- Successful delivery and deployment of at least one study scaffold/stent at intended target lesion
- Successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA)
- No in-hospital (maximum 7 days) TLF
1-Year TLF Components

- TLF: Absorb (7.8%) vs. XIENCE (6.1%), P=0.16
- Cardiac death: Absorb (0.6%) vs. XIENCE (0.1%), P=0.29
- TV-MI: Absorb (6.0%) vs. XIENCE (4.6%), P=0.18
- ID-TLR: Absorb (3.0%) vs. XIENCE (2.5%), P=0.50
ABSORB III Target Lesion Failure at 1 Year

Target-Lesion Failure (%)

Month since Index Procedure

Absorb: 7.7%

XIENCE: 6.0%

$P = 0.15$
ABSORB III Device Thrombosis to 1-Year Numerically Higher Stent Thrombosis Rates with BVS

Timing of Device Thrombosis

- **Device Thrombosis (Def/Prob)**
  - **Early (0 to 30 days)**: 0.7%
  - **Acute (≤ 24 hr)**: 0.6%
  - **Subacute (> 24 hr to 30 days)**: 0.9%
  - **Late (> 30 days to 1 year)**: 0.5%

- **P-value**
  - 0.13
  - 0.46
  - 0.19
  - 0.04
  - 0.10
## Device Thrombosis to 1 Year

<table>
<thead>
<tr>
<th></th>
<th>Absorb (N=1322)</th>
<th>Xience (N=686)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device Thrombosis (def*/prob)</td>
<td>1.54%</td>
<td>0.74%</td>
<td>0.13</td>
</tr>
<tr>
<td>- Early (0 to 30 days)</td>
<td>1.06%</td>
<td>0.73%</td>
<td>0.46</td>
</tr>
<tr>
<td>- Late (&gt; 30 to 1 year)</td>
<td>0.46%</td>
<td>0.00%</td>
<td>0.10</td>
</tr>
<tr>
<td>- Definite* (1 year)</td>
<td>1.38%</td>
<td>0.74%</td>
<td>0.21</td>
</tr>
<tr>
<td>- Probable (1 year )</td>
<td>0.15%</td>
<td>0.00%</td>
<td>0.55</td>
</tr>
</tbody>
</table>

*One “definite ST” in the Absorb arm by ITT was in a pt that was treated with Xience*
## Powered Secondary Endpoints

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Absorb (N=1322)</th>
<th>Xience (N=686)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>18.3%</td>
<td>18.4%</td>
<td>0.93</td>
</tr>
<tr>
<td>All Revascularization</td>
<td>9.1%</td>
<td>8.1%</td>
<td>0.50</td>
</tr>
<tr>
<td>ID-TVR</td>
<td>5.0%</td>
<td>3.7%</td>
<td>0.21</td>
</tr>
</tbody>
</table>
Summary and Conclusions (1)

- ABSORB BVS was non-inferior to Xience CoCr-EES for TLF at 1 year (primary endpoint met)
- TLF components (cardiac death, TV-MI, ID-TLR) were not significantly different between devices
- Angina, all revascularization and ID-TVR were similar between devices
- No statistically significant differences in device thrombosis were present
• The ABSORB III trial has demonstrated safety and efficacy of Absorb BVS at 1 year in patients with stable CAD and stabilized ACS

• Longer term evaluation is ongoing to determine if ABSORB improves late outcomes compared to Xience
Stone ABSORB 1-Year Meta-analysis: ST
ABSORB II, ABSORB III, ABSORB Japan, ABSORB China

<table>
<thead>
<tr>
<th>Event Type</th>
<th>BVS (N=2164)</th>
<th>CoCr-EES (N=1225)</th>
<th>RR [95% CI] Fixed effect</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device thrombosis (def/prob)</td>
<td>1.3%</td>
<td>0.6%</td>
<td>2.09 [0.92, 4.75]</td>
<td>0.08</td>
</tr>
<tr>
<td>- Definite</td>
<td>1.1%</td>
<td>0.5%</td>
<td>2.06 [0.85, 5.03]</td>
<td>0.11</td>
</tr>
<tr>
<td>- Probable</td>
<td>0.2%</td>
<td>0.1%</td>
<td>2.28 [0.28, 18.51]</td>
<td>0.44</td>
</tr>
<tr>
<td>- Early (0-30 days)</td>
<td>0.9%</td>
<td>0.5%</td>
<td>1.76 [0.72, 4.34]</td>
<td>0.22</td>
</tr>
<tr>
<td>- Late (30 days - 1 year)</td>
<td>0.4%</td>
<td>0.1%</td>
<td>4.10 [0.52, 32.56]</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Numerically higher event rates at every time point with BVS

NA = not applicable - cannot test for heterogeneity because no events were present in one cell in 3 of the 4 trials; het = heterogeneity
## Summary of BVS Meta-Analyses

<table>
<thead>
<tr>
<th>SAFETY</th>
<th>EFFICACY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cassese Meta-Analysis</strong> (includes ACS)</td>
<td><strong>Angiographic Outcomes</strong></td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>Def/Prob ST</td>
</tr>
<tr>
<td>ABSORB: 5.2%</td>
<td>ABSORB: 1.2%</td>
</tr>
<tr>
<td>XIENCE: 3.5%</td>
<td>XIENCE: 0.5%</td>
</tr>
<tr>
<td>$P=0.06$</td>
<td>$P=0.05$</td>
</tr>
<tr>
<td><strong>Stone Meta-Analysis</strong> (excludes ACS)</td>
<td>TV-MI:</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td></td>
</tr>
<tr>
<td>ABSORB: 5.5%</td>
<td>-</td>
</tr>
<tr>
<td>XIENCE: 4.1%</td>
<td>- ABSORB: 5.1%</td>
</tr>
<tr>
<td>$P=0.07$</td>
<td>- XIENCE: 3.3%</td>
</tr>
<tr>
<td></td>
<td>- $P=0.04$</td>
</tr>
<tr>
<td>Def/Prob ST</td>
<td>ABSORB: 1.3%</td>
</tr>
<tr>
<td>XIENCE: 0.6%</td>
<td>XIENCE: 0.6%</td>
</tr>
<tr>
<td>$P=0.08$</td>
<td>$P=0.08$</td>
</tr>
<tr>
<td>TLF</td>
<td></td>
</tr>
<tr>
<td>ABSORB: 5.1%</td>
<td>ABSORB: 6.6%</td>
</tr>
<tr>
<td>XIENCE: 5.1%</td>
<td>XIENCE: 5.1%</td>
</tr>
<tr>
<td>$P=0.04$</td>
<td>$P=0.04$</td>
</tr>
</tbody>
</table>

2.5 mm vessels may have skewed the data

- Both meta-analyses showed similar results (ST, MI higher with BVS)
- ST differences reached statistical significance in larger Cassese analysis which included all BVS RCTs
Outcomes by QCA RVD 2.25 mm

RVD <2.25 mm (mean 2.09 ± 0.24 mm)

RVD ≥2.25 mm (mean 2.80 ± 0.38 mm)

TLF: P_int diff = 0.31
TVMI: P_int diff = 0.09
ST: P_int diff = 0.12
**OCT Findings in BVS Thrombosis**

Quantitative and qualitative analysis of ST present in 14 BVS patients

8 Cases:
Early ST (<8 days)
- 2 Insufficient platelet inhibition
- 4 procedural factors (underexpansion, undersizing, geographical miss)
- 2 unknown

7 Cases:
Late/Very Late ST (<1 month/>1 year)
- 5 Intimal neovessels or marked peri-strut low intensity areas (PSLIA)
- 2 fractures found
- 1 scaffold collapse

Mechanisms of early ST are similar to metallic stents (mechanical and inadequate antiplatelet therapy). The predominant finding in late and very late ST is peri-strut low intensity area.
Can future generations of BRS overcome the challenges?

**Second Generation Design Considerations**
- Improved deliverability
- Thinner struts
- Increased overexpansion capability
- Fracture resistance
Departing pearls...

The Abbott BVS fully bioresorbable stent demonstrated non-inferiority to 3rd generation metallic stents at one year.

The bioresorbable stent represents a dramatic advancement in interventional cardiovascular medicine.

The Abbott bioresorbable stent will likely be approved in 2016.
THANK YOU

Watch over your heart with all diligence, for from it flows the springs of life. Proverbs 4:23

Visit us at www.centennialheart.com
### Design
- 1,189 patient single arm, ‘real world’ registry of the Absorb BVS at 10 European centres
- Primary outcome TLF at 1 year
- Composite of cardiac death, TV-MI, clinically driven TLR

### Baseline demographics and clinical characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>62.2 ± 11.0</td>
</tr>
<tr>
<td>Diabetes Mellitus (%)</td>
<td>24.8</td>
</tr>
<tr>
<td>Hyperlipidaemia (%)</td>
<td>52.9</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>73.5</td>
</tr>
<tr>
<td>Family history CAD (%)</td>
<td>38.8</td>
</tr>
<tr>
<td>Stable angina (%)</td>
<td>52.6</td>
</tr>
<tr>
<td>STEMI (%)</td>
<td>16.1</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>53.4</td>
</tr>
</tbody>
</table>

### Key lesion and procedural characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYNTAX score (n)</td>
<td>11.3 ± 7.9</td>
</tr>
<tr>
<td>A/B1 (%)</td>
<td>48.8</td>
</tr>
<tr>
<td>B2/C (%)</td>
<td>51.2</td>
</tr>
<tr>
<td>De novo lesions (%)</td>
<td>96.6%</td>
</tr>
<tr>
<td>CTO (%)</td>
<td>7.8</td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>19.4 ± 7.9</td>
</tr>
<tr>
<td>Pre-dil target lesion (%)</td>
<td>83.3 ± 13.9</td>
</tr>
<tr>
<td>Post-dilation (%)</td>
<td>49</td>
</tr>
<tr>
<td>IVUS/OCT (%)</td>
<td>28.2%</td>
</tr>
</tbody>
</table>
GHOST-EU Registry Results
Real World Outcomes with ABSORB BVS (N = 1,189 Patients)

*TLF includes cardiac death, myocardial infarction (MI) related to target vessel and clinically driven TLR.

**TVF includes cardiac death, target vessel MI, or clinically driven TVR

Thank you!