Bioabsorbable Scaffolds: The Next Holy Grail?

New Cardiovascular Horizons
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Rationale for the Development of Bioresorbable Vascular Scaffolds

• Limitations of metallic stents
  – restenosis
  – stent thrombosis
  – chronic inflammation
  – imaging artifacts
  – jailed side branches
  – inhibition of positive remodeling (shear stress adaptation)
  – prevention of normal physiologic function such as vasomotion
  – need for prolonged anti-platelet therapy
  – permanent implant complicating repeat intervention

Adapted from Waksman R. Update on bioabsorbable stents: From bench to bedside. J Interven Cardiol 2006;19:414-421.
<table>
<thead>
<tr>
<th>Device</th>
<th>Study</th>
<th>Drug</th>
<th>Lesions</th>
<th>n</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>Igaki-Tamai FIM</td>
<td>Igaki-Tamai</td>
<td>none</td>
<td>coronary</td>
<td>50</td>
<td>18% restenosis @ 12-months 28% TLR @ 10-years</td>
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<td>PROGRESS AMS</td>
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<td>63</td>
<td>48% restenosis @ 12-months</td>
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<td>BIOSOLVE-I</td>
<td>BIOSOLVE-I</td>
<td>paclitaxel</td>
<td>coronary</td>
<td>22</td>
<td>10% restenosis @ 6-months</td>
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<td>BIOSOLVE-I</td>
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<td>none</td>
<td>coronary</td>
<td>24</td>
<td>in-scaffold LLL 0.52 mm @ 12-months</td>
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<tr>
<td>RESORB</td>
<td>RESORB</td>
<td>none</td>
<td>coronary</td>
<td>30</td>
<td>67% TLR @ 6-months</td>
</tr>
<tr>
<td>RESTORE I</td>
<td>RESTORE I</td>
<td>none</td>
<td>coronary</td>
<td>22</td>
<td>2 MACE @6-months</td>
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<tr>
<td>ABSORB Cohort A</td>
<td>ABSORB Cohort A</td>
<td>everolimus</td>
<td>coronary</td>
<td>30</td>
<td>12% restenosis @ 6-months</td>
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<td>ABSORB Cohort B</td>
<td>ABSORB Cohort B</td>
<td>everolimus</td>
<td>coronary</td>
<td>45</td>
<td>2.4% restenosis @ 6-months</td>
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<td>ABSORB Extend</td>
<td>ABSORB Extend</td>
<td></td>
<td></td>
<td>56</td>
<td>3.5% restenosis @ 12-months</td>
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<tr>
<td>DESolve I</td>
<td>DESolve I</td>
<td>novolimus</td>
<td>coronary</td>
<td>15</td>
<td>0% restenosis @6-months</td>
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Abbott Vascular Everolimus Eluting Bioresorbable Vascular Scaffold Components

<table>
<thead>
<tr>
<th>Scaffold</th>
<th>Coating</th>
<th>Drug</th>
<th>Delivery system</th>
</tr>
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<tbody>
<tr>
<td>Bioresorbable</td>
<td>Bioresorbable</td>
<td>Everolimus</td>
<td>XIENCE V</td>
</tr>
<tr>
<td>• Poly(L-lactide) (PLLA)</td>
<td>• Poly(L,L-lactide) (PDLLA) coating</td>
<td>• Similar dose density and release rate to XIENCE V</td>
<td>• World-class deliverability</td>
</tr>
<tr>
<td>• Naturally resorbed, fully metabolized</td>
<td>• Naturally resorbed, fully metabolized</td>
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</table>

Photos taken by and on file at Abbott Vascular.
Representative photomicrographs of porcine coronary arteries, 2x

Absorb™ v. Cypher®

Photos taken by and on file at Abbott Vascular.

Tests performed by and data on file at Abbott Vascular.
Post-procedure

Pre-procedure

Diameter

Area

A

B

C

D

E

Dmin 2.63 mm
Dmax 3.05 mm
Dmean 2.83 mm
<table>
<thead>
<tr>
<th></th>
<th>26 lesions</th>
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</thead>
<tbody>
<tr>
<td><strong>Pre-procedure</strong></td>
<td></td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>8.66</td>
</tr>
<tr>
<td>RVD (mm)</td>
<td>2.78</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>1.10</td>
</tr>
<tr>
<td>DS (%)</td>
<td>59%</td>
</tr>
<tr>
<td><strong>Post-procedure</strong></td>
<td></td>
</tr>
<tr>
<td>In-stent MLD (mm)</td>
<td>2.33</td>
</tr>
<tr>
<td>In-stent DS (%)</td>
<td>16%</td>
</tr>
<tr>
<td>In-stent acute gain (mm)</td>
<td>1.24</td>
</tr>
<tr>
<td><strong>6-mos. follow-up</strong></td>
<td></td>
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<tr>
<td>In-stent MLD (mm)</td>
<td>1.88</td>
</tr>
<tr>
<td>In-stent DS (%)</td>
<td>27%</td>
</tr>
<tr>
<td><strong>In-stent late loss (mm)</strong></td>
<td><strong>0.44 ± 0.35</strong></td>
</tr>
<tr>
<td>In-stent ABR (%)</td>
<td>11.5%</td>
</tr>
</tbody>
</table>
Comparison of DES - Late Lumen Loss

In-stent late loss (mm)
• Lower MCUSA (maximum unsupported scaffold area)
• More even support of arterial wall
• More uniform strut distribution
• Lower late stent area loss
• Improved stent retention
• Unchanged material and strut thickness


**Radial Strength**

Figure 5. Acute radial strength data for ABSORB Cohort B (3.0 x 18 mm), XIENCE V (3.0 x 18 mm), Cypher Select (3.0 x 18 mm), and Taxus Liberté (3.0 x 20 mm) \((n = 5\) for each set) obtained using the MSI RX550 radial expansion force gauge. Tests were performed by and data are on file at Abbott Vascular.

Ormiston J, Serruys PW. ABSORB Cohort B Trial – Two year clinical and angiographic results of the ABSORB everolimus eluting bioresorbable vascular scaffold (poster). Transcatheter Cardiovascular Therapeutics; 2011 November 8; San Francisco, CA.
Angiographic late lumen loss – two-year results


Ormiston J, Serruys PW. ABSORB Cohort B Trial – Two year clinical and angiographic results of the ABSORB everolimus eluting bioresorbable vascular scaffold (poster). Transcatheter Cardiovascular Therapeutics; 2011 November 8; San Francisco, CA.

**Absorb™ v. XIENCE V® at 2-years**

**Graph:**
- **ABSORB™ BVS(B1+B2)**
- **XV®(3.0 x 18mm subgroup, SPI+SPII+SPIII RCT)**

**758-day HR**
- 0.97 [0.42,2.21]
- p=0.9379

**MACE (C-Death, MI, ID-TLR)**

Time Post Index Procedure (Months)

<table>
<thead>
<tr>
<th>Days</th>
<th>0</th>
<th>37</th>
<th>194</th>
<th>284</th>
<th>393</th>
<th>573</th>
<th>758</th>
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<tr>
<td>Absorb™</td>
<td>101</td>
<td>99</td>
<td>96</td>
<td>96</td>
<td>93</td>
<td>91</td>
<td>41</td>
</tr>
<tr>
<td>XIENCE V®</td>
<td>227</td>
<td>224</td>
<td>219</td>
<td>211</td>
<td>204</td>
<td>202</td>
<td>191</td>
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</tbody>
</table>

Rapoza R. Absorb BVS Program: Long-term experimental data angiography, IVUS, OCT, histology and micro CT. Local Drug Delivery and Cardiovascular Course on Revascularisation; 2012 February 4; Geneva, Switzerland. ABSORB and XIENCE V are trademarks of the Abbott Group of Companies.
QCA post procedure

Post procedure

Preprocedure

FUP before vasomotion

5 Min. After Methergine

After Nitro

MLD 2.45mm

Late Loss: -0.01mm

Minimal LD 1.58 mm
Mean LD 2.12 mm

Mean LD ∆-0.60mm (-22%)

Minimal LD 2.46 mm
Mean LD 2.72 mm

Mean LD ∆+0.55mm (+26%)

Minimal LD 2.32 mm
Mean LD 2.67 mm

Mean LD (∆-0.01mm)
Recovery of Vasoreactivity after Absorb Implantation

ABSORB Cohort B - Late Lumen Enlargement by IVUS

Ormiston J, Serruys PW. ABSORB Cohort B Trial – Two year clinical and angiographic results of the ABSORB everolimus eluting bioresorbable vascular scaffold (poster). Transcatheter Cardiovascular Therapeutics; 2011 November 8; San Francisco, CA.
Study Objective
Continued Access trial. FPI: Jan 11, 2010

Endpoints
Typical PCI clinical endpoints

Treatment
Up to 2 *de novo* lesions in different epicardial vessels
Planned overlapping allowed in lesions >22 and ≤ 28 mm

Device Sizes
Scaffold diameters: 2.5, 3.0, 3.5 mm
Scaffold lengths: 12*, 18, 28 mm

Bartorelli, A, An Interim Report on the 12-Month Clinical Outcomes from the First 250 Patients Registered, and An Interim Report on the 6-Month Clinical Outcomes from the First 500 Patients Registered, TCT 2012

Bartorelli, A. An Interim Report on the 12-Month Clinical Outcomes from the First 250 Patients Registered, and An Interim Report on the 6-Month Clinical Outcomes from the First 500 Patients Registered, TCT 2012

ABSORB III + IV Clinical Trial Program

ABSORB III

2,250 pts with up to 2 de novo lesions in different epicardial vessels enrolled, with follow-up for at least 5 years, at up to 122 US and non-US sites

2,000 pts randomized 2:1 ABSORB v XIENCE (+50 lead-in pts and 200 pt non-randomized angio/IVUS/OCT/VM FU cohort)

RVD: 2.50 - 3.75 mm; Lesion length: ≤24 mm

Scaffold diameters: 2.5, 3.0 and 3.5 mm
Scaffold lengths: 12, 18, and 28 mm

Primary endpoint (n=2,000):
TLF at 1 year (powered for noninferiority) – US approval

PIs: SG Ellis, DJ Kereiakes
Study chairman: GW Stone

TCT2012
The ABSORB Clinical Trials

• Use online QCA
• Avoid under sizing, as postdilation is limited to 0.5 mm
• Proper lesion preparation = sufficient large balloon (min 2.5 mm)
• Use more supportive wires
• Direct stenting possible in ACS

<table>
<thead>
<tr>
<th>Device</th>
<th>Company</th>
<th>Study</th>
<th>Drug</th>
<th>Lesions</th>
<th>n</th>
<th>Status</th>
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<tbody>
<tr>
<td>DREAMS AMS</td>
<td>Biotronik</td>
<td>BIOSOLVE I</td>
<td>paclitaxel</td>
<td>coronary</td>
<td>56</td>
<td>in-scaffold LLL 0.52 mm @12-months</td>
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<tr>
<td>ReZOLVE</td>
<td>Reva Medical, Inc.</td>
<td>RESTORE I</td>
<td>none</td>
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<td>2 MACE @6-months</td>
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<td></td>
<td></td>
<td>RESTORE II</td>
<td>sirolimus</td>
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<td>125</td>
<td>enrolling</td>
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<tr>
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<td>ABSORB III</td>
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<td>Elixir Medical</td>
<td>DESolve I</td>
<td>novolimus</td>
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<td>16</td>
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<td>DESolve Nx</td>
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<td>enrolled</td>
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</table>
The Resorbable Holy Grail

- Restoration of normal vasomotion, with NO production
- Restoration of normal shear stress and cyclic strain
- Restoration of normal vessel curvature
- Reduced risk of very late polymer reactions
- Avoidance/resolution of positive remodeling and stent malapposition
- Avoidance/resolution of late strut fractures

- Less neoatherosclerosis
- Un-jailing of side-branches
- Plaque regression
- MRI/CT imaging follow-up
- The return of normal vessel architecture