ABSORB Bioresorbable Vascular Scaffold System

- The 4th Revolution in Interventional Cardiology

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Abbott Vascular

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Presentation Outline

- Introduction and History of Interventional Cardiology
- The 4th revolution - Absorb Bioresorbable Vascular Scaffold System
  - The Clinical Need for a Bioresorbable Vascular Scaffold
  - Design Goals of a Bioresorbable Vascular Scaffold
  - Device Design and Technology
  - ABSORB Clinical Program and Studies
  - Summary
Introduction and History of Interventional Cardiology
Coronary Artery Disease (CAD) and Chest Pain: Chronic Angina, Unstable Angina or Acute MI
What a myocardial infarction looks like in the heart …

Acute anteroseptal infarction (Front)

Healed posterior infarction with overlying thrombus (Back)
CAD is the number one leading cause of mortality worldwide for patients 60 years and older.

Deaths in patients aged >60 years globally (2002)\(^1\)

Gold standard to diagnose CAD: Coronary angiography

**Technique**
- Catheter into coronary artery
- Catheter entrance

**Anatomy**
- Right Coronary Artery
- LAD: Left Anterior Descending Artery

**Angiogram**
- LAD
Left Coronary Artery with Atherosclerotic Stenosis
Natural Progression of Coronary Artery Disease

Factors:
- Local factors (ESS)
- Systemic factors
- Genetic factors

Factors:
- Local factors (ESS)
- Systemic factors
- Genetic factors

TCFA

Unstable Angina

Acute MI

Asymptomatic

Stable Angina

Glagov Phenomenon


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Interventional Cardiology – The beginning

1977

1. Balloon (PTCA):
Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

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Restenosis after Balloon Angioplasty (PTCA)

Pre PTCA

Immediately post - PTCA

6-month restenosis post - PTCA
Interventional Cardiology – The 2nd revolution

1977
1. Balloon (PTCA): Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

1988
2. Bare Metal Stent (BMS): Julio Palmaz and Richard Schatz develop a stainless steel stent for coronary applications
Restenosis after Stenting
Interventional Cardiology entering the 3rd revolution

1977
1. Balloon (PTCA):
   Andreas Gruntzig performs the first PTCA in Zurich, Switzerland

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2. Bare Metal Stent (BMS):
   Julio Palmaz and Richard Schatz develop a stainless steel stent for coronary applications

2002 - 2003
3. Drug-eluting stents (DES):
   introduced to the European and U.S. markets
Interventional Cardiology entering the 4th revolution

1977
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2002 - 2003
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   introduced to the European and U.S. markets

2011
4. Absorb
   Bioresorbable Vascular Scaffold (BVS)
Absorb Bioresorbable Vascular Scaffold (BVS) – The 4th Revolution

The Clinical Need for a Bioresorbable Vascular Scaffold
‘Caged’ (Stented) Vessel

- Benign NIH
- In-Stent Restenosis
- Neo-Atheroma $\rightarrow$ Stent Thrombosis?
- Delayed Healing $\rightarrow$ Stent Thrombosis?
- Late Acquired Malapposition $\rightarrow$ Stent Thrombosis?

1. Virmani, R. CIT 2010

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Since struts disappear, issues related to very late persistent strut malapposition and chronically uncovered struts become irrelevant.
The Clinical Need for a Bioresorbable Vascular Scaffold

Rationale

Vessel scaffolding is only needed transiently*

Vision

Improve Long Term Outcomes for Patients by Leaving No Scaffold Behind\(^1\)

Potential Benefits

- Restore the vessel to a more natural state, capable of natural vascular function
- Eliminate chronic sources of vessel irritation and inflammation
- Vessels remain free for future treatment options
- Reduce the need for prolonged DAPT\(^2\)
- Allows for use of non-invasive imaging techniques (CCTA)
- Improve patient quality of life

* Serruys PW, et al., Circulation 1988; 77: 361. Serial study suggesting vessels stabilize 3-4 months following PTCA.
\(^1\) Small platinum markers at scaffold edges remain for fluoroscopic landmarking. 2. The Absorb IFU indicates DAPT for a minimum of 6 months.
Absorb Bioresorbable Vascular Scaffold (BVS)

Design Goals of a Bioresorbable Vascular Scaffold
What is Required of a Fully Bioresorbable Scaffold ???

Revascularization  Restoration  Resorption

1  3  6  Mos  2 Yrs

Platelet Deposition
Leukocyte Recruitment
SMC Proliferation and Migration
Matrix Deposition
Re-endothelialization
Vascular Function


*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.

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Potential for Mechanical Conditioning

Gradual disappearance of supportive scaffold

Vessel recovers the ability to respond to physiologic stimuli
- Shear stress & pulsatility
- Tissue adaptation
- Structure and functionality

Support

Vascular Function

Restoration and Resorption

Mechanical conditioning may lead to improved cellular organization and vascular function

Absorb Bioresorbable Vascular Scaffold (BVS)

Device Design and Technology
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

*Except for platinum markers
All illustrations are artists' renditions

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Bioresorbable Polymer

**Everolimus/PDLLA Matrix Coating**
- Thin layer
- Amorphous (non-crystalline)
- 1:1 ratio of Everolimus/PDLLA matrix
- Conformal coating, 2-4 μm thick
- Controlled drug release

**PLLA Scaffold**
- Semi-crystalline
- Provides device structure
- Processed for required radial strength
Absorb Bioresorbable Vascular Scaffold: Three Phases of Functionality

- Revascularizes like a best-in-class DES, XIENCE
- Enables natural vessel function for improved long-term outcomes
- Resorbs in a benign fashion with no inflammation or irritation, leaving no scaffold behind*

Early evidence of vasomotion indicates return to natural vessel function with the potential of improved long-term outcomes

Vascular Reparative Therapy (VRT)

*Small platinum markers at scaffold edges remain for fluoroscopic landmarking.
Absorb Vessel Support Over Time

Absorb appears to maintain adequate support for at least as long as is needed

Devices subjected to simulated physiologic environment (fatigue testing). Tests performed at and data on file at Abbott Vascular.

Absorb Conformability

Absorb provides better conformability compared to metallic platforms

Serruys, PW. TCT 2009; J. Gomez-Lara, JACC Cardiovascular Interventions

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Hydrolysis randomly cleaves amorphous tie chains, leading to a decrease in molecular weight without altering radial strength.

When enough tie chains are broken, the device begins losing radial strength.

Illustration is artist’s rendition. Data on file at Abbott Vascular.

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The Absorb BVS Scaffold is Replaced by Functional Cellular Matrix


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Porcine Coronary Artery Safety Study Demonstrates Biocompatibility

BVS Cohort A Device

Resorption Site

Polymer is replaced by provisional matrix

1 month 6 months 1 year 2 years 3 years 4 years

Representative Photomicrographs, Hematoxylin and Eosin, 2x objective

Tests performed by Abbott Vascular.
Data and images on file at Abbott Vascular.

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The final golden tube – visualized by OCT (Optical Coherence Tomography)

Images courtesy of Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands, ABSORB A 5 yr

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Absorb Bioresorbable Vascular Scaffold (BVS)

ABSORB Clinical Program and Studies
Absorb: A Revolutionary Therapy
Building Evidence

First in Man
• Cohort A
• Cohort B

Expanding Experience
• ABSORB Extend

Novel Endpoints
• ABSORB II

Pivotal Trials and Land Mark Analysis
• ABSORB III / IV
• ABSORB Japan
• ABSORB China
**Study Objective**
First In Man, Single Arm – safety/performance

**Endpoints**
Typical PCI clinical and imaging endpoints

**Treatment**
Single, de novo native coronary lesion in a vessel with a reference vessel diameter of 3.0 mm

**Device Sizes**
3.0 x 12 mm scaffolds (3.0 x 18 mm scaffolds available after enrolment start and used in 2 pts)

**Introduction**
**ABSORB Cohort A**

30 subjects (Non-randomized) 4 sites in Europe & New Zealand

Follow-Up (Months) 6 12 18 24 36 48 60

QCA, IVUS, OCT, IVUS VH MSCT

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ABSORB Cohort A
Excellent Long-Term Data Out to 5 Years

ABSORB Cohort A Clinical Results at Each Phase: Intent to Treat

<table>
<thead>
<tr>
<th>Hierarchical</th>
<th>6 Months 30 Patients</th>
<th>1 year 29 Patients**</th>
<th>2 Year 29 Patients**</th>
<th>5 Year 29 Patients**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemia Driven MACE***</td>
<td>1 (3.3%)*</td>
<td>1 (3.4%)*</td>
<td>1 (3.4%)*</td>
<td>1 (3.4%)*</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>MI</td>
<td>1 (3.3%)*</td>
<td>1 (3.4%)*</td>
<td>1 (3.4%)*</td>
<td>1 (3.4%)*</td>
</tr>
<tr>
<td>Q-Wave MI</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Non Q-Wave MI</td>
<td>1 (3.3%)*</td>
<td>1 (3.4%)*</td>
<td>1 (3.4%)*</td>
<td>1 (3.4%)*</td>
</tr>
<tr>
<td>Ischemia Driven TLR by PCI</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>by CABG</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

No scaffold thrombosis by ARC or Protocol

* Same patient – this patient also underwent a TLR, not qualified as ID-TLR (DS = 42%)
** One patient withdrew consent and missed the 9, 12, 18 month and 2, 3, and 4 year visits; two patients died from a non-cardiac causes, one at 706 days and one at 888 days post procedure
*** MACE – Composite endpoint comprised of cardiac death, myocardial infarction (MI) and ischemia-driven target lesion revascularization (TLR) by PCI or CABG

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Serruys, TCT, 2011
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ABSORB Cohort A
OCT Images – Baseline, 6 months and 2 years

Serruys, PW., ESC 2008.
Late lumen loss at 6 months mainly due to reduction in scaffold area

Very late lumen enlargement noted from 6 months to 2 years

*Adapted from Serruys, PW, ACC 2009.
BVS Device Optimization Objectives

More uniform strut distribution
More even support of arterial wall
⇒ Lower late scaffold area loss (Late loss)
   Maintain radial strength for at least 3 months

Unchanged:
   Material, coating and backbone
   Strut thickness
   Drug release profile
Study Objective
First In Man, Single Arm – safety/performance

Endpoints
Typical PCI clinical and imaging endpoints

Treatment
Up to 2 *de novo* lesions in different epicardial vessels
Reference vessel diameter of 3.0 mm, lesions ≤ 14 mm in length

Device Sizes
3.0 x 18 mm devices

101 subjects
(Non-randomized) 12 sites in Europe, Australia, New Zealand

Group B1 (n = 45)

Imaging Follow-Up (Months)
6 12 18 24 36

Group B2 (n = 56)
QCA, IVUS, OCT, IVUS VH
MSCT
## ABSORB Cohort B Group 1&2
### Clinical Results - Intent to treat

<table>
<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>6 Months</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non -Hierarchical</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac Death %</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Myocardial Infarction % (n)</strong></td>
<td>2.0 (2)</td>
<td>3.0 (3)</td>
<td>3.0 (3)</td>
<td>3.0 (3)</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Non Q-wave MI</td>
<td>2.0 (2)</td>
<td>3.0 (3)</td>
<td>3.0 (3)</td>
<td>3.0 (3)</td>
</tr>
<tr>
<td><strong>Ischemia driven TLR % (n)</strong></td>
<td>0</td>
<td>2.0 (2)</td>
<td>4.0 (4)</td>
<td>6.0 (6)</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PCI</td>
<td>0</td>
<td>2.0 (2)</td>
<td>4.0 (4)</td>
<td>6.0 (6)</td>
</tr>
<tr>
<td><strong>Hierarchical MACE % (n)</strong></td>
<td>2.0 (2)</td>
<td>5.0 (5)</td>
<td>6.9 (7)</td>
<td>9.0 (9)</td>
</tr>
</tbody>
</table>

No scaffold thrombosis by ARC or Protocol out to 2 – Year only 2 additional TLR events between 1 year and 2 year

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D. Dudek, ACC 2012 / *One patient missed the 2 year FUP

MACE: Cardiac death, MI, ischemia-driven TLR
TVF: Cardiac death, MI, ischemia-driven TLR, ischemia-driven TVR

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Similar Rates of MACE Compared to Historical XIENCE Data

Intent to Treat (ITT) Analysis; Interim Snapshot

ABSORB Cohort B
Temporal Lumen Dimensional Changes

Pre-PCI  | Post-PCI  | 6 Months  | 2 Years  
---|---|---|---

**Lumen Area**

- Pre-PCI: 6.53 mm²
- Post-PCI: 6.36 mm²
- 6 Months: 6.36 mm²
- 2 Years: 6.85 mm²

**Scaffold Area**

- Pre-PCI: ↓ 1.7%
- Post-PCI: ↑ 7.2%
- 6 Months: ↑ 7.2%
- 2 Years: ↑ 7.2%

**Very late lumen enlargement noted from 6 months to 2 years**

*Serruys, PW., TCT 2011
ABSORB Vasomotor Function Testing:
Restoration of Vasomotion

6 Months
ABSORB Cohort B1
(n=15)

12 Months
ABSORB Cohort B2
(n=19)

24 Months
ABSORB Cohort A
(n=9)

- Vasodilation
- Vasoconstriction


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ABSORB EXTEND
Non-Randomized, Single-Arm, Continued Access Trial

Study Objective
Continued Access trial. FPI: Jan 11, 2011

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

* Sizes to be introduced into the trial once available.

~1,000 subjects
Up to 100 global sites (non-US)

Clinical Follow-Up
Clinical Follow-up (months) 6 12 18 24 36

MSCT follow up (n=100)
OCT follow up (n=50)

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### ABSORB Extend
Clinical Results - Intent to treat; Interim Snapshot

<table>
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<tr>
<th></th>
<th>30 Days* n = 451</th>
<th>6 Months* n = 269</th>
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<td><strong>Cardiac Death (%)</strong></td>
<td>0 (0.0)</td>
<td>1 (0.4)**</td>
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<td><strong>Myocardial Infarction n (%)</strong></td>
<td></td>
<td></td>
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<tr>
<td>Q-wave MI</td>
<td>3 (0.7)</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Non Q-wave MI</td>
<td>7 (1.6)</td>
<td>4 (1.5)</td>
</tr>
<tr>
<td><strong>Ischemia Driven TLR n (%)</strong></td>
<td></td>
<td></td>
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<tr>
<td>PCI</td>
<td>1 (0.2)</td>
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<tr>
<td>CABG</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Hierarchical MACE n (%)</strong></td>
<td>10 (2.2)</td>
<td>8 (3.0)</td>
</tr>
</tbody>
</table>

*Reflects an interim snapshot with only cleaned data as of the cut-off date of Jan. 11, **A non-BVS was implanted in the target lesion 2012
MACE: cardiac death, MI, ischemia-driven TLR
RJ van Geuns, PCR Rotterdam 2012
**Study Objective**
Randomized against XIENCE PRIME control. FPI 28-Nov-2011

- Vasomotion assessed by change in Mean Lumen Diameter between pre- and post-nitrate at 2 years (superiority)
- Minimum Lumen Diameter (MLD) at 2 years post nitrate minus MLD post procedure post nitrate (non-inferiority, reflex to superiority)

**Co-primary Endpoints**

**Treatment**
Up to 2 de novo lesions in different epicardial vessels
Planned overlapping allowed in lesions ≤ 48 mm

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

* Non-German sites only.
** Sizes to be introduced into the trial once available.
ABSORB III
US Approval Trial

Study Objective
Seek US approval of Absorb BVS

Primary Endpoint
Clinically indicated target lesion failure at 1-year (composite of cardiac death, target vessel MI or clinically indicated TLR)

Treatment
Up to two de novo lesions in different epicardial vessels. No planned overlap allowed

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

~2000 subjects (1267 Absorb, 733 XIENCE)
US and Australian sites. Follow-up out to 5 years

Clinical follow-up

<table>
<thead>
<tr>
<th>Follow-Up (Months)</th>
<th>1</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
<th>36</th>
<th>48</th>
<th>60</th>
</tr>
</thead>
</table>

PRO follow-up

IVUS/OCT/Vasomotion follow-up (N~200 US subjects)
Summary

Current clinical data for the Absorb BVS suggest three phases of functionality:

1. **Revascularization** with comparable safety and efficacy outcomes to best in class DES (drug eluting stent)
   - No ST in ABSORB Cohort A (5 year follow up)\(^1\) and Cohort B (2 year follow up)\(^3\);
   - 0.4% ST at 6 months in ABSORB EXTEND\(^4\)
   - Comparable MACE rates (3.4% at 5 years (Cohort A)\(^1\), 9.0% at 2 years (Cohort B)\(^3\), and 2.9% at 6 months – Extend\(^4\))

2. **Restoration**: First signs by showing
   - Possible restoration of vasomotion function
     - (19/33 patients had increasing MLD post Acetylcholine – Cohort B)\(^2\)
   - Possible late lumen gain between 6 and 24 months (Cohort B)\(^1\)

3. **Resorption** of Absorb has been shown on OCT, resulting in the final “golden tube”

\(^{1}\) Serruys, PW., TCT 2011; \(^{2}\) J. Ormiston, TCT 2011; \(^{3}\) D. Dudek, ACC 2012; \(^{4}\) RJ van Geuns, EuroPCR BVS focus Rotterdam 2012;
* Images courtesy of Thoraxcenter, Erasmus MC, Rotterdam, The Netherlands, ABSORB A 5 yr
Thank you!

Questions?