From ABSORB Cohort A to ABSORB III and IV Randomized Trials

Stephen G. Ellis, M.D.
Professor of Medicine
Director Invasive Services
Co-Director Cardiac Gene Bank

Cleveland Clinic
Disclosures

- Consultant, Abbott Vascular
- Co-Principal Investigator, ABSORB III and IV
Bioabsorbable Coronary Scaffold

Potential Benefits

• Minimize Neoatherosclerosis -> Less late stent thrombosis
• Restore normal vasomotor responses -> Less low shear distally -> less atherosclerosis; better peak exercise capacity
• Doesn’t block CABG (esp LIMA to LAD)
• Allows better non-invasive CT evaluation
Delayed Healing - DES

Lack of neointimal growth (uncovered struts)

Persistent fibrin deposition

Rabbit 28 days

CYPHER

Severe inflammation

Incomplete endothelialization

Porcine 28 days

Fibrin deposition with stent malapposition

TAXUS

Virmani et al.
SIRTAX-LATE: Target Lesion Revascularization

Landmark analysis

Raber L et al. Circulation. 2011;123:2819-2828
Bern Rotterdam (n=12,339 pts)
ARC Definite or Probable ST at 4 Years

Cumulative incidence (%)

Months after index PCI

EES vs. SES HR = 0.41 (0.27–0.62), \( P<0.0001 \)
EES vs. PES HR = 0.33 (0.23–0.48), \( P<0.0001 \)

No. at risk

<table>
<thead>
<tr>
<th></th>
<th>PES</th>
<th>SES</th>
<th>EES</th>
</tr>
</thead>
<tbody>
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<td>3753</td>
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<td>2456</td>
<td>1025</td>
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<td>42</td>
<td>1034</td>
<td>2061</td>
<td>505</td>
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<tr>
<td>48</td>
<td>660</td>
<td>1687</td>
<td>203</td>
</tr>
</tbody>
</table>

Lorenz Ršber, ESC 2011
Neoatherosclerosis and Time From Stent Implant

Nakazawa et al., JACC Img 2009;2:625-8

SGE; 0412-10, 11
BVS: Absorption Seen by OCT and Pathology

By chromatography, polymeric struts were no longer detectable.

Strut voids were filled with young connective tissue and coalesced with vessel wall.

collagen = yellow
proteoglycans/mucopolysaccharides = blue/green
SMCs = red

density of smooth muscle cells at the presumed site of polymeric struts.

Serruys et al., the Netherlands, 2011
Abbott BVS

Expectations

- Parity versus current DES early
- Superiority versus DES late
ABSORB Global Clinical Program

Building the Evidence

First in Man
• Cohort A
• Cohort B

Expanding Experience
• ABSORB Extend
• ABSORB BTK

Novel Endpoints
• ABSORB II
• ABSORB Physiology

Pivotal Trials and Landmark Analysis
• ABSORB RCT
• ABSORB Japan
• ABSORB China
ABSORB Cohort A

Principal Investigators:
Patrick Serruys, John Ormiston

- Prospective, open label, single arm study
- 30 patients enrolled at 4 sites
- Device sizes: 3.0 x 12 mm; 3.0 x 18 mm in two patients
- Treatment: single *de novo* lesion
- Follow-up schedule:
  - QCA, OCT, IVUS, VH
  - 30 d, 6 mo, 12 mo, 24 mo, 36 mo, 48 mo, 60 mo

MSCT follow-up
**ABSORB Cohort A**

**Temporal Changes in Lumen**

<table>
<thead>
<tr>
<th>Time</th>
<th>Lumen Area</th>
<th>Scaffold Area</th>
<th>IVUS n</th>
<th>Unpaired Analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-PCI</td>
<td>6.04 mm²</td>
<td></td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>6 Mos.</td>
<td>5.19 mm²</td>
<td>↓ 11.8%</td>
<td>25</td>
<td>11.8%</td>
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<td>24 Mos.</td>
<td>5.46 mm²</td>
<td>↑ 10.85%</td>
<td>18</td>
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</table>

Angiographic Late Loss = 0.43 mm

- Late lumen loss at 6 months mainly due to reduction in scaffold area
- Very late lumen enlargement noted from 6 months to 2 years

*Serruys, PW., TCT 2008*
Non-invasive CT imaging for early and late follow-up is now feasible
### ABSORB A – 5Y Clinical Results

<table>
<thead>
<tr>
<th>Hierarchical</th>
<th>6 Months</th>
<th>12 Months</th>
<th>5 Years</th>
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<tr>
<td></td>
<td>30 Patients</td>
<td>29 Patients*</td>
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<tr>
<td>Ischemia Driven MACE, % (n)</td>
<td>3.3% (1)*</td>
<td>3.4% (1)**</td>
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<td>Cardiac Death, %</td>
<td>0.0%</td>
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<td>MI, % (n)</td>
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<td>Q-Wave MI</td>
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<td>Ischemia Driven TLR, % by PCI</td>
<td>0.0%</td>
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<td>by CABG</td>
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- No new MACE events between 6 months and 5 years
- No scaffold thrombosis up to 5 years

*consent withdrawn after 6 months; **Non-ID-TLR (DS<42%) w/ post-procedural non-Q MI
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Device Optimization Objectives

- More uniform strut distribution
- More even support of arterial wall
- Maintain radial strength for at least 3-4 months
- Storage at room temperature
- Improved device retention
- Unchanged:
  - Material, coating and backbone
  - Strut thickness
  - Drug release profile
  - Total degradation Time

Photos taken by and on file at Abbott Vascular.
ABSORB Cohort B

Principal Investigators:
John Ormiston, Patrick Serruys

- Prospective, open label, single arm study
- 101 patients enrolled at 12 sites
- Device sizes: 3.0 x 18 mm
- Treatment: up to 2 \textit{de novo} lesion
- Follow-up schedule:

Group B1 (n = 45)
Group B2 (n = 56)
MSCT follow-up

Baseline  6 mo  12 mo  18 mo  24 mo  36 mo  48 mo  60 mo
### ABSORB Cohorts A and B: Temporal Changes in Lumen Dimensions

#### Post-PCI

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Lumen Area</th>
<th>Scaffold Area</th>
<th>Late Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABSORB</strong></td>
<td>6.04 mm²</td>
<td>↓ 11.8%</td>
<td>0.43 mm</td>
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</table>

#### 6 Mos.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Mean Lumen Area</th>
<th>Scaffold Area</th>
<th>Late Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABSORB</strong></td>
<td>6.36 mm²</td>
<td>↓ 1.7%</td>
<td></td>
</tr>
<tr>
<td><strong>Cohort A</strong></td>
<td>6.19 mm²</td>
<td></td>
<td></td>
</tr>
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<td><strong>Cohort B</strong></td>
<td>6.85 mm²</td>
<td>↑ 7.2%</td>
<td></td>
</tr>
</tbody>
</table>

#### 24 Mos.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Mean Lumen Area</th>
<th>Scaffold Area</th>
<th>Late Loss</th>
</tr>
</thead>
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<tr>
<td><strong>ABSORB</strong></td>
<td>6.85 mm²</td>
<td></td>
<td></td>
</tr>
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<td><strong>Cohort A</strong></td>
<td>6.53 mm²</td>
<td></td>
<td></td>
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<td>6.19 mm²</td>
<td></td>
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</table>

*Serruys, PW., TCT 2008

**Serruys, PW., TCT 2011
Evolution of LL Cumulative Curves – 6 Months

ABSORB BVS vs. XIENCE V (non-matched population)

6M EES (SPIRIT I): 0.10±0.23 mm (N=22)

6M BVS (Cohort B): 0.19±0.18 mm (N=42)

ABSORB BVS is neither approved nor available for sale in the U.S.
Evolution of LL Cumulative Curves – 12 Months

ABSORB BVS vs. XIENCE V (non-matched population)

12M EES (SPIRIT I): 0.23 ± 0.29 mm (N=22)

12M BVS (Cohort B): 0.27 ± 0.25 mm (N=56)

ABSORB BVS is neither approved nor available for sale in the U.S.
Evolution of LL Cumulative Curves – 24 Months

ABSORB BVS vs. XIENCE V (non-matched population)

- EES 24M
  - 24M EES (SPIRIT II): $0.33 \pm 0.37$ mm (N=96)

- ABSORB 24M
  - 24M BVS (Cohort B): $0.27 \pm 0.20$ mm (N=38)

Serruys, PW., TCT 2011

ABSORB BVS is neither approved nor available for sale in the U.S.
Return of Vasomotor Function

Cohort B1
(n=15)

Cohort B2
(n=6)

Cohort A
(n=19)

6 Months

12 Months

24 Months

Vessel Diameter (mm)

Δ in Vessel Diameter (pre-drug infusion to post-drug infusion)

Acetylcholine
Methergine

1Adapted from Serruys, PW. ACC 2011
2Adapted from Serruys, PW. ACC 2011
## ABSORB Cohort B1

### Clinical Results up to 2 Years

<table>
<thead>
<tr>
<th>Outcome</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Hierarchical</strong></td>
<td>N=45</td>
<td>N = 44*</td>
</tr>
<tr>
<td>Cardiac Death %</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial Infarction % (n)</td>
<td>2.2 (1)</td>
<td>2.3 (1)</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>0</td>
<td>0</td>
</tr>
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<td>2.2 (1)</td>
<td>2.3 (1)</td>
</tr>
<tr>
<td>Ischemia driven TLR %</td>
<td>4.4 (2)</td>
<td>4.5 (2)</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>PCI</td>
<td>4.4 (2)</td>
<td>4.5 (2)</td>
</tr>
<tr>
<td>Hierarchical MACE % (n)</td>
<td>6.7 (3)</td>
<td>6.8 (3)</td>
</tr>
</tbody>
</table>

*1 patient missed the 2-year visit

**MACE**: Cardiac death, MI, ischemia-driven TLR

---

**No scaffold thrombosis by ARC or Protocol**
### ABSORB Cohort B1
### Clinical Results up to 2 Years

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*1 patient missed the 2-year visit

**MACE:** Cardiac death, MI, ischemia-driven TLR

**No scaffold thrombosis by ARC or Protocol**
ABSORB Cohort B, (n=101) vs. patients treated with a single 3x 18 mm XIENCE V (SPIRIT First+II+III, n=227)

ABSORB BVS is neither approved nor available for sale in the U.S.

Dudek. ACC 2012
Importance of Accurate Vessel Sizing: ABSORB Cohort B Case Study

Pre BVS

After 3.0mm BVS implantation before post-dilatation

After 4.0 mm post-dilatation

Ormiston Circ Interv 2011
Probability of Single Strut Abnormality

Risk of single strut fracture during post-dilatation (3.0 mm device)

- IFU Post-Dil Max = 3.5 mm

Avg. Scaffold Inner Diameter 1 atm Prior to Fracture (mm)
ABSORB EXTEND

Principal Investigator: Alexandre Abizaid
Co-PI: Antonio Bartorelli; Rob Whitbourn

- Continued Access trial. FPI*: Jan 11, 2010
- No hypothesis-testing, typical PCI endpoints, 1000 patients
- Device Sizes: 2.5, 3.0 mm (diameters); 18, 28 mm (lengths)
- Lesion lengths ≤ 28 mm
- Planned overlap allowed
- Two imaging subgroups: OCT (n=50, planned overlap only); MSCT (n=100)
- Follow-up schedule:
  
  Clinical follow-up
  
  30 d  6 mo  12 mo  24 mo  36 mo

  MSCT follow-up (n=100)
  OCT follow-up (n=50)
**ABSORB EXTEND vs Cohort B vs SPIRIT Pooled (SPIRIT I + II + III)**:
Protocol MACE K-M curves up to 12 Months

### Protocol MACE

<table>
<thead>
<tr>
<th>Days After Index Procedure</th>
<th>0</th>
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<th>194</th>
<th>393</th>
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<tbody>
<tr>
<td>BVS EXTEND at Risk</td>
<td>469</td>
<td>440</td>
<td>260</td>
<td>112</td>
</tr>
<tr>
<td>ABSORB Cohort B at Risk</td>
<td>101</td>
<td>99</td>
<td>96</td>
<td>94</td>
</tr>
<tr>
<td>SPIRIT Pooled at Risk</td>
<td>482</td>
<td>475</td>
<td>462</td>
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Note: ABSORB Extend is based on data from data cut off date of January 11, 2012. Only clean and adjudicated data is shown.

Note: Due to the interim nature of this analysis, FU data is not available for every subject at every timepoint.

*SPIRIT Pooled is defined as those subjects receiving either a 3.0 x 18 mm, 2.5 x 18 mm, or 3.0 x 28 mm XIENCE V stent from the SPIRIT FIRST + SPIRIT II + SPIRIT III trial populations.*
**ABSORB EXTEND vs Cohort B vs SPIRIT Pooled (SPIRIT I + II + III)**: Protocol MACE K-M curves up to 12 Months

**Early excess risk, then flattening of the MACE curve vs DES**

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**ABSORB-RCT**

**ABSORB III (N~2300)**

- **PI:** Steve Ellis, Dean Kereiakes
- **Objective:** For US approval of BVS
- **Primary Endpoint:** Target Lesion Failure (TLF) at 1 year, non-inferiority to XIENCE V/PRIME

**ABSORB IV (N~3000)**

- **PI:** Gregg Stone
- **Co-PI:** Steve Ellis, Dean Kereiakes
- **Objective:** For label claims
- **Major Sec. Endpoint:** Landmark analysis on TLF from 1 to 5 years, superiority to XIENCE V/PRIME
ABSORB-U.S. RCT

Some Key Issues Still Under Discussion

1) What is the proper definition of peri-procedural MI (drives sample size)?
2) How should predilatation strategy be prescribed and if different than usual, when should patient be randomized?
3) Given U.S. practice of not usually using QCA for vessel sizing, what strategy/training is needed to assure proper BVS sizing?
ABSORB-U.S. RCT

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To Start Approximately December 2012!