12-month clinical and 13-month angiographic outcomes from a randomized trial evaluating the Absorb Bioresorbable Vascular Scaffold vs. metallic drug-eluting stent in de novo native coronary artery lesions

ABSORB JAPAN

Takeshi Kimura M.D. and Gregg W. Stone M.D. on behalf of the ABSORB Japan Investigators
DECLARATION OF INTEREST

- Research contracts
- Consulting/Royalties/Owner/ Stockholder of a healthcare company
Study Backgrounds

Theoretically, bioresorbable vascular scaffolds (BVS) may overcome the shortcomings of permanent metallic prosthesis.

However, whether BVS are as safe and effective as metallic DES prior to complete bioresorption is currently unknown.

Therefore, a randomized, controlled trial comparing the clinical and angiographic outcomes of BVS with those of Xience cobalt-chromium everolimus-eluting stents (CoCr-EES) was designed to support regulatory approval of the Absorb BVS in Japan.
**ABSORB Japan**

Prospective, randomized, active control, single-blind, non-inferiority, multi-center Japanese study

**Inclusion:** Patients with up to 2 *de novo* target lesions in separate native coronary arteries
Lesion length ≤ 24 mm, \(D_{\text{max}} \geq 2.5 \text{ mm to } \leq 3.75 \text{ mm}, \%\text{DS} \geq 50\% \text{ to } <100\%\)

**Exclusion:** AMI, EF <30\%, eGFR <30 mL/min/1.73m\(^2\),
LMCA, Ostial lesion, Excessive vessel tortuosity, Heavy calcification, Myocardial bridge, Bifurcation with side branch ≥2 mm

**Primary Clinical Endpoint:** Target Lesion Failure (TLF): Cardiac death, TV-MI, ID-TLR at 12 months

**Major Secondary Angiographic Endpoint:** In-segment Late Lumen Loss at 13 months

**Randomized 2:1**

**BVS**
Tx. with single study device
Diameter: 2.5, 3.0, 3.5 mm
Length: 8, 12, 18, 28 mm

**CoCr-EES**
Tx. with single study device
Diameter: 2.5, 3.0, 3.5 mm
Length: 8, 12, 18, 28 mm
Randomized (N=400)

Withdraw consent without POCE: 1

Intention-to-treat Population (N=398)

Enrollment from 38 Japanese centers
Between April 27, 2013 and December 27, 2013

Withdraw consent without POCE: 1

12-Month Clinical FU Complete (N=397: 99.7%)

13-Month Angiographic FU Qualified (N=378: 95.0%)

BVS (N=266)

CoCr-EES (N=134)

BVS (N=265)

CoCr-EES (N=133)

BVS (N=264)

CoCr-EES (N=133)

BVS (N=252)

CoCr-EES (N=126)
### Baseline Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>BVS (266 Patients)</th>
<th>CoCr-EES (134 Patients)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>67.1 ± 9.4</td>
<td>67.3 ± 9.6</td>
<td>0.90</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>79%</td>
<td>74%</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>24.0 ± 3.0</td>
<td>24.3 ± 3.0</td>
<td>0.41</td>
</tr>
<tr>
<td><strong>Current Tobacco Use</strong></td>
<td>20%</td>
<td>22%</td>
<td>0.69</td>
</tr>
<tr>
<td><strong>Stable CAD</strong></td>
<td>90%</td>
<td>84%</td>
<td>0.054</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>36%</td>
<td>36%</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>Prior PCI/CABG</strong></td>
<td>36%</td>
<td>38%</td>
<td>0.70</td>
</tr>
<tr>
<td><strong>Prior MI</strong></td>
<td>16%</td>
<td>24%</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>eGFR &lt;60 (mL/min)</strong></td>
<td>32%</td>
<td>28%</td>
<td>0.37</td>
</tr>
</tbody>
</table>
Device success: Successful deployment of the assigned device at the target lesion with <30% residual stenosis

Procedure success: Device success without TLF during the hospital stay (maximum of 7 days)
# Post Procedural QCA

<table>
<thead>
<tr>
<th></th>
<th>BVS (275 Lesions)</th>
<th>CoCr-EES (137 Lesions)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVD Post (mm)</td>
<td>2.75 ± 0.42</td>
<td>2.85 ± 0.43</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>In-Device MLD Post (mm)</strong></td>
<td><strong>2.43 ± 0.37</strong></td>
<td><strong>2.64 ± 0.40</strong></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>In-Device %DS Post (%)</td>
<td>11.6 ± 7.5</td>
<td>7.3 ± 8.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>In-Segment MLD Post (mm)</strong></td>
<td><strong>2.20 ± 0.39</strong></td>
<td><strong>2.27 ± 0.43</strong></td>
<td>0.15</td>
</tr>
<tr>
<td>In-Segment %DS Post (%)</td>
<td>20.0 ± 6.7</td>
<td>20.6 ± 8.80</td>
<td>0.49</td>
</tr>
<tr>
<td>In-Device Acute Gain (mm)</td>
<td>1.47 ± 0.40</td>
<td>1.65 ± 0.40</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>In-Segment Acute Gain (%)</td>
<td>1.25 ± 0.41</td>
<td>1.28 ± 0.45</td>
<td>0.49</td>
</tr>
</tbody>
</table>
Primary Endpoint:
12-Month TLF (through 393 days)

The one-sided upper 95% confidence limit for the 0.39% observed difference in event rates was 3.95%, suggesting that any absolute difference between the 2 devices is likely to be small.

NI Margin = 8.6%
Non-inferiority P < 0.0001
## 12-Month Clinical Outcomes (~393-Day)

<table>
<thead>
<tr>
<th>Event Description</th>
<th>BVS (N=266)</th>
<th>CoCr-EES (N=134)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLF (CD/TV-MI/ID-TLR)</td>
<td>4.2% (11/265)</td>
<td>3.8% (5/133)</td>
<td>0.85</td>
</tr>
<tr>
<td>- Cardiac Death</td>
<td>0.0% (0/265)</td>
<td>0.0% (0/133)</td>
<td>1.00</td>
</tr>
<tr>
<td>- Target Vessel MI</td>
<td>3.4% (9/265)</td>
<td>2.3% (3/133)</td>
<td>0.76</td>
</tr>
<tr>
<td>- Ischemia driven-TLR</td>
<td>2.6% (7/265)</td>
<td>2.3% (3/133)</td>
<td>1.00</td>
</tr>
</tbody>
</table>
12-Month Definite/Probable ST

<table>
<thead>
<tr>
<th></th>
<th>0 days</th>
<th>37 days</th>
<th>208 days</th>
<th>393 days</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BVS at Risk</strong></td>
<td>266</td>
<td>262</td>
<td>260</td>
<td>257</td>
</tr>
<tr>
<td><strong>CoCr-EES at Risk</strong></td>
<td>134</td>
<td>132</td>
<td>131</td>
<td>131</td>
</tr>
</tbody>
</table>

HR [95% CI] = 1.01 [0.18, 5.49]

p = 0.99 (Log rank test)
Major Secondary Angiographic Endpoint: 13-Month In-Segment LLL

13-Month In-segment LLL

- BVS: 0.13 mm
- CoCr-EES: 0.12 mm

P = 0.74

Upper 95% Confidence Limit of the Difference

- Difference (BVS - CoCr-EES) = 0.01 mm
- Upper 95% UCL = 0.07 mm
- NI Margin = 0.195 mm

Non-inferiority P < 0.0001

Asymptotic test statistic based on Z test
Cumulative Distribution Function Curves for In-segment MLD

Pre
0.96±0.33 mm
0.99±0.36 mm
P=0.42

Follow-up
2.08±0.45 mm
2.15±0.50 mm
P=0.18

Post
2.21±0.39 mm
2.26±0.43 mm
P=0.19
ABSORB Japan

Study Limitations

1. Large non-inferiority margin for the primary clinical endpoint, particularly with event rate lower than anticipated
   - ABSORB Japan was designed to support regulatory approval of the Absorb BVS in Japan. The Japanese Regulatory Agency requested a clinical primary endpoint and agreed to a relatively large non-inferiority margin to keep the study sample size reasonable.
   - Although TLF rates of both BVS and CoCr-EES were lower than the anticipated rate of 9%, the 0.39% observed difference (P=0.85) suggest that the 2 devices are similar.

2. Underpowered to evaluate the low frequency events such as ST

3. Inclusion of a highly selected patient population
   - The study provides data for a patient population typical of pivotal studies for approval.
   - Data in broader patient populations will be studied in subsequent trials.
Conclusions

In the ABSORB Japan trial, BVS demonstrated a similar mid-term (12-month) clinical safety and efficacy profile as CoCr-EES, with comparable 13-month angiographic outcomes.

These positive results lay a solid foundation for continued evaluation of long term outcomes in patients undergoing percutaneous coronary intervention with Absorb BVS.
A randomized trial evaluating everolimus-eluting Absorb bioresorbable scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: ABSORB Japan

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