Emerging Cardiac Technologies

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Financial Disclosures

None
Examples of Emerging Technologies

**Therapeutic**
- Bioabsorbable Stents
- Transcatheter Mitral Valve Repair
- Left Atrial Appendage Occlusion
- Transcatheter Aortic Valve Replacement (TAVR)
- Stem Cell Therapy
- Left Ventricular Assist Device
- Cardiac Arrhythmia Ablation (Cryoablation and RFA)

**Diagnostic**
- Physiologic Assessment of Coronary Stenoses (iFR/FFR)
- IVUS/OCT
- Remote Rhythm Monitoring
- POC Testing
- Genomic Testing
Examples of Emerging Technologies

**Therapeutic**
- Bioabsorbable Stents
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- POC Testing
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Bioabsorbable Stents: Problems with Bare Metal and Drug Eluting Metal Stents

- Permanently implanted – “I don’t want that in me forever!”
- Risk of stent thrombosis: subacute, late and “very late” stent thrombosis
  - Need for indefinite anti-platelet therapy?
- Rigid scaffold impairs physiologic vasoreactivity and endothelial function
- Presence of permanent stents may
  - Indefinitely compromise side branches
  - Limit ability to perform future CABG.
  - Impair non-invasive imaging (e.g., CT Angiography)

J Am Coll Cardiol 2008;52:1134-1140
Angioplasty without permanent stenting can be a successful and durable procedure!

Limitations
- Acute: vessel closure from dissection
- Intermediate: elastic recoil
- Long-term: restenosis (neointimal hyperplasia)

Stents were developed in large measure to combat these adverse events and in so doing greatly improved long-term results.

Promise of Bioabsorbable Stents

Rationale

Vessel scaffolding is only needed transiently*

Vision

Improve Long Term Outcomes for Patients by Leaving No Scaffold Behind

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
- 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.
What is the Minimum Duration of Radial Support?

Restenosis rarely occurs beyond 3 months after coronary angioplasty.

The lumen appears to stabilize approximately three months after PTCA.

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
ABSORB
First In Man Clinical Trial

- Implantation of BVS stents in native coronary arteries
- 2 different Cohorts
- ABSORB Cohort A: 30 patients enrolled March – July 2006
  - Only one coronary lesion, 60 month follow-up
- ABSORB Cohort B: 101 patients enrolled March – November 2009
  - Up to 2 coronary lesions (in different arteries), 36 month follow-up
# ABSORB

## Follow-up Data

### ABSORB Cohort A

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>1 (3.4%)*</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>MI</td>
<td>1 (3.4%)*</td>
</tr>
<tr>
<td>Q-Wave MI</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Non Q-Wave MI</td>
<td>1 (3.4%)*</td>
</tr>
<tr>
<td>Ischemia Driven TLR by PCI</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Ischemia Driven TLR by CABG</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

### ABSORB Cohort B

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MACE</td>
<td>9 (9.0%)</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>MI</td>
<td>3.0 (3)</td>
</tr>
<tr>
<td>Q-Wave MI</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Non Q-Wave MI</td>
<td>3.0 (3)</td>
</tr>
<tr>
<td>Ischemia Driven TLR by PCI</td>
<td>6 (6.0%)</td>
</tr>
<tr>
<td>Ischemia Driven TLR by CABG</td>
<td>6 (6.0%)</td>
</tr>
<tr>
<td>Ischemia Driven TLR by CABG</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
ABSORB
Vasoreactivity

ABSORB Cohort A at 2 years

Acetylcholine (Vasodilator)

Methergine (Vasoconstrictor)

2 Year Follow-up Vasomotion Results

Vasodilation

Vasoconstriction
GHOST-EU Registry

Is Absorb™ BVS Ready for Routine Clinical Practice?

1189 patient single arm, ‘real world’ registry of the ABSORB BVS

Authors conclude “scaffold thrombosis rate resembles that of first-generation DES, suggesting a negative impact of high strut thickness on this event.”
SYNERGY Stent

**Current DES**
Conformable Durable Polymer

**SYNERGY DES**
Abluminal Bioerodable Polymer

+6 months

Arterial Wall

*Everolimus + Ultra-thin Bioerodable PLGA Polymer applied to abluminal aspect of a 0.0028” stent strut*
EVOLVE Trial (SYNERGY Stent)
Revascularization and ST at 6 Months

<table>
<thead>
<tr>
<th></th>
<th>PROMUS Element</th>
<th>SYNERGY</th>
<th>SYNERGY ½ Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TVR</strong></td>
<td>6.1</td>
<td>3.2</td>
<td>2.1</td>
</tr>
<tr>
<td><strong>TLR</strong></td>
<td>3.1</td>
<td>1.1</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Non-TLR TVR</strong></td>
<td>3.1</td>
<td>2.2</td>
<td>1.0</td>
</tr>
<tr>
<td><strong>Stent Thrombosis</strong></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

All P=N.S
EVOLVE Trial (SYNERGY Stent)
Death and MI at 6 Months

Patients, %

0 0 0 0 0 0

All Death Cardiac Death Noncardiac Death All MI Q-Wave Non-Q-Wave

All P=N.S.

PROMUS Element SYNERGY SYNERGY ½ Dose
EVOLVE Trial (SYNERGY Stent)
Target Lesion Failure

30 days

- PROMUS Element: 0%
- SYNERGY: 1.1%
- SYNERGY ½ Dose: 3.1%

6 Months

- PROMUS Element: 3.1%
- SYNERGY: 2.2%
- SYNERGY ½ Dose: 4.1%
Conclusions

• In this prospective, randomized, multicenter, First Human Use trial, the two dose formulations of the SYNERGY stent were non-inferior to the PROMUS Element stent for the primary angiographic endpoint of in-stent late loss at 6 months.
  – Clinical events were low and comparable with no stent thromboses in any group.
• These results support the safety and efficacy of the novel abluminal bioabsorbable polymer SYNERGY everolimus-eluting stent for the treatment of patients with de novo coronary artery disease.
• Additional research is needed to evaluate clinical event rates and the potential for dual antiplatelet therapy reduction with this novel stent.
Transcatheter Mitral Valve Repair

Valvular Heart Disease: Incidence

Prevalence of Valvular Heart Disease by Age


Severity of MR and Survival

Note: Adjusted survival estimates are shown.
Functional Mitral Regurgitation: Treatment options

Medical management
  - Symptom control
  - Doesn’t address underlying pathophysiology

Surgical (Repair/Replacement)
  - Effective but associated with significant morbidity/mortality
  - Minority of patients with significant functional MR undergo surgery
Catheter-Based Mitral Valve Repair
MitraClip® System
MitraClip Mechanical Effects

- Improves leaflet coaptation by tethering leaflets thus reducing the time and force required to close valve
- Reduces LV volume overload by reducing MR
- Creates a “tissue bridge”
- May limit annular dilatation
- Restrains LV wall and Limits LV dilatation
Endovascular Valve Edge-to-Edge REpair Study (EVEREST II)

Significant Mitral Regurgitation (3-4+)

Device Group
MitraClip System

Control Group
Surgical Repair/Replacement

Echocardiography Core Lab and Clinical Follow-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years
EVEREST II RCT: MR Reduction

Device Group

Baseline
n=137

12 Months
n=119

≤2+
81.5%

3+/4+
18.5%

Control Group

Baseline
n=80

12 Months
n=67

≤2+
97.0%
EVEREST II: Left Ventricular Volume

**Device Group**

- **Baseline**
- **12 Months**

**Control Group**

- **Baseline**
- **12 Months**

---

**Legend:**

- **LVEDV** = left ventricular end diastolic volume
- **LVESV** = left ventricular end systolic volume

- **p<0.0001**
- **p=0.0005**
- **p=0.0255**
EVEREST II NYHA: Functional Class

Device Group

Control Group

Baseline
12 months
Baseline
12 months

p<0.0001

p<0.0001

97.6% NYHA Class I/II

87.9% NYHA Class I/II

Percent Patients

I
II
III
IV
Percutaneous LAA Occlusion

Atrial Fibrillation

- Most common arrhythmia
- Markedly increased risk of embolic stroke
- Anticoagulation effective therapy but carries risk of hemorrhagic complications

What to do with patients who have contraindications for anticoagulation?

- Over 85% of strokes are embolic
- More than 90% of source of thrombus is felt to be from the LAA
Percutaneous LAA Occlusion

Indications in patients at high risk of stroke
- High risk (or recurrence) of bleeding with anticoagulation
- Ischemic stroke despite well-controlled anticoagulation therapy
- Non-compliance with anticoagulation
- Intolerance to anticoagulation drugs

Options
- Surgical ligation
- Percutaneous occlusion
  - PLAATO (no longer available)
  - Watchman (Protect AF Trial)
  - ACP
  - Coherex
PROTECT AF Clinical Trial Design

- Prospective, randomized study of WATCHMAN LAA Device vs. Long-term Warfarin Therapy
- 2:1 allocation ratio device to control
- 800 Patients
  - Device Group (463)
  - Control Group (244)
  - Roll-in Group (93)
- TEE follow-up at 45 days, 6 months and 1 year
- Clinical follow-up biannually up to 5 years
- Regular INR monitoring while taking warfarin
### PROTECT AF

**Primary Efficacy Results**

Randomization allocation (2 device : 1 control)

<table>
<thead>
<tr>
<th>Event-free probability</th>
<th>Device</th>
<th>Control</th>
<th>Posterior Probabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort</strong></td>
<td>Events (no.)</td>
<td>Total pt-yr</td>
<td>Rate (95% CI)</td>
</tr>
<tr>
<td>900 pt-yr</td>
<td>20</td>
<td>582.3</td>
<td>3.4 (2.1, 5.2)</td>
</tr>
</tbody>
</table>

**Event-free probability**

- **WATCHMAN**
- **Control**

**Days**

- **244**
- **147**
- **52**
- **12**

- **463**
- **270**
- **92**
- **22**
## PROTECT AF
### All Stroke

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Device Events</th>
<th>Total pt-yr Rate (95% CI)</th>
<th>Control Events</th>
<th>Total pt-yr Rate (95% CI)</th>
<th>RR (95% CI)</th>
<th>Posterior probabilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>600 pt-yr</td>
<td>14</td>
<td>409.3</td>
<td>3.4 (1.9, 5.5)</td>
<td>8</td>
<td>223.6</td>
<td>3.6 (1.5, 6.3)</td>
</tr>
<tr>
<td>900 pt-yr</td>
<td>15</td>
<td>582.9</td>
<td>2.6 (1.5, 4.1)</td>
<td>11</td>
<td>318.1</td>
<td>3.5 (1.7, 5.7)</td>
</tr>
</tbody>
</table>

**Event-free probability**

**WATCHMAN**

**Control**

**Non-inferior**
Physiologic Assessment of Coronary Stenoses (iFR/FFR)

Fractional Flow Reserve (FFR)
- Assessment of “Functional Significance” of a coronary stenosis
- Measures pressure gradient across a stenosis during peak hyperemia
- Strongly validated as the “Gold Standard” for assessing the physiologic significance of a coronary stenosis.

Instant Wave-Free Ratio (iFR)
- Measures change in pressure (i.e., change in flow) across a coronary stenosis during a diastolic portion of the cardiac cycle
  - If Resistance is stable, pressure ~ flow
- Measures functional significance without the need to administer vasodilating drugs (adenosine).
Fractional Flow Reserve versus Angiography for Multivessel Evaluation

FRACTIONAL FLOW RESERVE versus ANGIOGRAPHY FOR GUIDING PCI IN PATIENTS WITH MULTIVESSEL CORONARY ARTERY DISEASE

Stenting of non-ischemic stenoses has no benefit compared to medical treatment only.

Stenting of ischemia-related stenoses improves symptoms and outcomes in multivessel coronary disease.

Identifying which stenoses cause ischemia is difficult:

*Non-invasive tests are often unreliable in MVD and coronary angiography often results in both under- or overestimation of functional stenosis severity.*

**Fractional Flow Reserve (FFR),** is the most accurate and selective index to indicate whether a particular stenosis is responsible for ischemia.
FAME study

absolute difference in MACE-free survival

Survival Free of MACE

Days since Randomization

FFR-guided

Angio-guided

30 days
2.9%

90 days
3.8%

180 days
4.9%

360 days
5.3%

Ref. NEJM Vol 360, No 3, pp 213-224.
Instant Wave-Free Ratio (iFR):
Naturally occurring diastolic wave-free period
ADVISE Study

**ADenosine Vasodilation Independent Stenosis Evaluation Study**
- First in man pilot study

Microvascular Resistance during the wave-free period is:
- Similar in **stability** to that induced by adenosine over the whole cycle
- Similar in **magnitude** to that induced by adenosine over the whole cycle
- iFR has close diagnostic match with FFR – across all subgroups
Clinical implications of iFR

- Promote physiologically guided revascularization
- Applicable to a wider patient population
- Improved work-flow in catheter lab
- Improves patient experience
Questions?