Drug-eluting Stents in 2007

**TAXUS**
- Paclitaxel
- Polyolefin derivative
- Express$^2$

**Cypher**
- Sirolimus
- PEVA + PBMA blend
- BX Velocity
LaST – Late DES Stent Thrombosis After 3 Years

Baseline

Late Stent Thrombosis at 3.5 yrs

After 2 DES
Pathology Findings - Sirolimus-Eluting Stents from Different Coronary Arteries in the Same Patient (delayed healing)

BMS 24 Months after Deployment

Cypher 16 Months after Deployment

Incomplete Strut Endothelialization With DES?

Sirolimus-eluting stent

Bare metal stent

Angioscopy at 8 months post SES implantation

Virmani autopsy data

Kotani J et al. JACC. 2006,47:2108

59 Year Old Female with TAXUS Stent in the LAD for 130 Days

Eosinophils

Giant cells

Fibrin

80% surface endothelialized

Late Incomplete Apposition

Drug-eluting stent group

Baseline

Follow-up

... vulnerable struts at the time when antiplatelets may not be taken
Late incomplete apposition and Cypher ® stent thrombosis

Pre

Post

6 m

18 m
Late incomplete apposition and Cypher® stent thrombosis
Stent thrombosis 20 months after sirolimus-eluting stent implantation: **Strut fracture**

Lee MS et al. AJC/TCT2006
When should TAXUS or CYPHER be used (rather than BMS)?

- **“On-label” use**
  - Single *de novo* lesion in a native coronary artery in patients with stable CAD
  - Cypher: 2.5-3.5 mm RVD, ≤30 mm long
  - Taxus: 2.5-3.75 mm RVD, ≤28 mm long

- **“Off-label” use**
  - Everything else – multiple lesions and multiple vessels, bifurcation lesions, left main disease, thrombus and AMI, SVGs, CTOs, etc.
Analysis of All Patients
RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS

All Patients
(n=1,748)
RVD 2.5 – 3.5 mm
Length ≤30 mm

Control
(n=870)
Morice MC et al. NEJM 2002;346:1773-80
Moses JW et al. NEJM 2003;349:1315-23

CYPHERER
(n=878)
Schampaert E et al. JACC 2004;43:1110–5
Analysis of All Patients
TAXUS I, II, IV, V, VI

All Patients
(n=3,506)
RVD 2.25 – 4.0 mm
Length ≤46 mm

Control
(n=1,757)
Stone GW et al. NEJM 2004;350:221-31

TAXUS
(n=1,749)
Stone GW et al. JAMA 2005;294:1215-23
Dawkins KD et al. Circulation 2005;112:3306-3313
9 Prospective, Double-Blind, Randomized Trials

Freedom From (Protocol) Stent Thrombosis

RAVEL, SIRIUS, E-SIRIUS, and C-SIRIUS
(n=1,748)

99.4% (5)  P=0.20
98.8% (10)

TAXUS I, II, IV, V, VI
(n=3,513)

99.1% (14)  P=0.30
98.7% (20)

Time after Initial Procedure (years)

Bare metal stent (n=878)
CYPHER stent (n=870)

Bare metal stent (n=1,758)
TAXUS stent (n=1,755)

Stone GW et al. NEJM 2007;356:998-1008
9 Prospective, Double-Blind, Randomized Trials
Freedom From (Protocol) Stent Thrombosis

RAVEL, SIRIUS, E-SIRIUS, and C-SIRIUS
(n=1,748)

TAXUS I, II, IV, V, VI
(n=3,513)

99.4% (5)
P=0.20
98.8% (10)

99.1% (14)
P=0.30
98.7% (20)

After 1 year
5 vs. 0, P=0.025

After 1 year
9 vs. 2, P=0.028

Bare metal stent (n=878)
CYPHER stent (n=870)

Bare metal stent (n=1,758)
TAXUS stent (n=1,755)

Stone GW et al. NEJM 2007;356:998-1008
9 Prospective, Double-Blind, Randomized Trials

Freedom From All Cause Death

**RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS**
(n=1,748)

- 94.7% (45) P=0.23
- 93.3% (57)

**TAXUS I, II, IV, V, VI**
(n=3,513)

- 93.9% (86) P=0.68
- 93.4% (92)

Time after Initial Procedure (years)

Bare metal stent (n=878)
CYPHER stent (n=870)
TAXUS stent (n=1,755)

Stone GW et al. NEJM 2007;356:998-1008
### 9 Prospective, Double-Blind, Randomized Trials

**Freedom From Myocardial Infarction**

- **RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS**
  - (n=1,748)
  - 93.8% (53)
  - 93.6% (55)
  - \( P = 0.86 \)

- **TAXUS I, II, IV, V, VI**
  - (n=3,513)
  - 93.7% (105)
  - 93.0% (115)
  - \( P = 0.66 \)

**Graphs**

- **Bare metal stent** (n=878)
- **CYPHER stent** (n=870)
- **TAXUS stent** (n=1,727)
9 Prospective, Double-Blind, Randomized Trials
Freedom From Ischemic TLR

RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS
(n=1,748)

TAXUS I, II, IV, V, VI
(n=3,513)

P<0.0001
92.2%  (66)
76.4%  (202)
P<0.0001
89.9%  (166)
80.0%  (338)

Bare metal stent (n=878)
CYPHER stent (n=870)
Bare metal stent (n=1,758)
TAXUS stent (n=1,755)

Stone GW et al. NEJM 2007;356:998-1008
# TLR up to 4 Years: Subgroup Summary

**TAXUS II, IV, V, VI Meta-analysis**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HR [95% CI]</th>
<th>HR</th>
<th>TAXUS</th>
<th>Control</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>0.46</td>
<td>10.3%</td>
<td>20.2%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>RVD ≤2.5</td>
<td>0.42</td>
<td>13.2%</td>
<td>27.8%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>RVD 2.5 - ≤3.0</td>
<td>0.49</td>
<td>9.8%</td>
<td>18.7%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>RVD &gt;3.0</td>
<td>0.53</td>
<td>7.3%</td>
<td>12.7%</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Lsn Length &lt;18</td>
<td>0.46</td>
<td>9.7%</td>
<td>19.1%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Lsn Length 18-26</td>
<td>0.48</td>
<td>11.0%</td>
<td>20.9%</td>
<td>0.0006</td>
<td></td>
</tr>
<tr>
<td>Lsn Length &gt;26</td>
<td>0.45</td>
<td>12.9%</td>
<td>26.6%</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Non-Diabetic</td>
<td>0.47</td>
<td>9.6%</td>
<td>18.7%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Diabetic-Oral</td>
<td>0.42</td>
<td>12.3%</td>
<td>25.7%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Diabetic-Insulin</td>
<td>0.45</td>
<td>13.6%</td>
<td>23.3%</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Single Stent</td>
<td>0.50</td>
<td>9.6%</td>
<td>17.4%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Multiple Stents</td>
<td>0.34</td>
<td>12.1%</td>
<td>32.5%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.44</td>
<td>9.5%</td>
<td>19.9%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.50</td>
<td>12.2%</td>
<td>20.8%</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
</tbody>
</table>
TAXUS II, IV, V, VI: Death and MI Within 7 Days of TLR and Stent Thrombosis

Total intent-to-treat population: 3445 patients

Control 1727
- Stent thrombosis
  - 14 pts
  - 12 patients with death or MI

- Ischemia-driven TLR
  - 290 pts
  - 11 patients with death or MI

TAXUS 1718
- Ischemia-driven TLR
  - 135 pts
  - 4 patients with death or MI

- Stent thrombosis
  - 20 pts
  - 19 patients with death or MI

Σ: 23 Pts with Death or MI
(4 Deaths + 21 MIs)

Σ: 23 Pts with Death or MI
(3 Deaths + 23 MIs)

Stone GW et al. Circulation in press
Cumulative Incidence of Stent Thrombosis at 4 Years

**Cypher (ARC Definite or Probable, 1° + 2°)**

<table>
<thead>
<tr>
<th>Days after Initial Procedure</th>
<th>No. at Risk</th>
<th>Sirolimus stent</th>
<th>Bare-metal stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>870</td>
<td>878</td>
<td>870</td>
</tr>
<tr>
<td>180</td>
<td>863</td>
<td>863</td>
<td>853</td>
</tr>
<tr>
<td>360</td>
<td>848</td>
<td>848</td>
<td>842</td>
</tr>
<tr>
<td>720</td>
<td>823</td>
<td>823</td>
<td>825</td>
</tr>
<tr>
<td>1080</td>
<td>788</td>
<td>788</td>
<td>788</td>
</tr>
<tr>
<td>1440</td>
<td>789</td>
<td>789</td>
<td>789</td>
</tr>
</tbody>
</table>

**Mauri L, et al. NEJM 2007; 356: 1020-29**
Cumulative Incidence of Stent Thrombosis at 4 Years

TAXUS (ARC Definite or Probable, $1^\circ + 2^\circ$)


P = 0.52

<table>
<thead>
<tr>
<th>Days after Initial Procedure</th>
<th>No. at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Paclitaxel stent</td>
</tr>
<tr>
<td>0</td>
<td>1400</td>
</tr>
<tr>
<td>180</td>
<td>1351</td>
</tr>
<tr>
<td>360</td>
<td>1300</td>
</tr>
<tr>
<td>720</td>
<td>1117</td>
</tr>
<tr>
<td>1080</td>
<td>715</td>
</tr>
</tbody>
</table>

Cumulative Incidence (%)

- Paclitaxel stent: 1.8%
- Bare-metal stent: 1.4%
De Novo Lesions

CRF DES Evidence-based Medicine Guidelines Summary 2007

De Novo Lesions

On-label use

Cypher
RVD 2.5 – 3.5 mm, LL ≤ 30 mm

Taxus
RVD 2.5 – 3.75 mm, LL ≤ 28 mm

*2.25 & 4.0 mm randomized subgroups of TAXUS-V; SIRIUS registries
DES: Off-label use

• More complex and unapproved indications
  - Very small vessels and very long lesions
  - Chronic total occlusions
  - Bifurcations
  - Left main disease
  - In-stent restenosis
  - Multivessel disease
  - Saphenous vein grafts
  - Acute myocardial infarction
DES: Off-label use

- More complex and unapproved indications

- Part II of my talk!