Current Status of Coronary Artery Disease Treatment

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Columbia University
New York, USA
7-year Angio FU from FIM (Sousa et al.)

pre
post
1year
2years
4years
7years
DES in Complex Lesions

- Diabetes
- Long lesions
- Small vessels
- Left main
- Multivessel disease
DES in Complex Lesions

- Diabetes
- Long lesions
- Small vessels
- Left main
- Multivessel disease
Study Design

Multi-center, prospective, randomized study of patients with non-insulin-dependent or insulin-dependent diabetes with de novo, native coronary stenosis (n = 160)

Randomized 1:1 stratified by diabetes treatment status: insulin-dependent (IDDM) or non–insulin-dependent (NIDDM)

Bare-Metal Stent (BMS) Group
Bx VELOCITY™
(n = 80 patients; 110 lesions)

SES Group
CYPHER®
(n = 80 patients; 111 lesions)

Primary Endpoint: in-segment late lumen loss assessed by quantitative coronary angiography (QCA) at 270 days

Sabaté M., et al., Circulation 2005; 112: 2175-83
## Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>BMS Group (n = 80)</th>
<th>SES Group (n = 80)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>67.2 ± 10</td>
<td>65.9 ± 9</td>
<td>0.38</td>
</tr>
<tr>
<td>Male (%)</td>
<td>62.5</td>
<td>62.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Insulin-Dependent (%)</td>
<td>33.8</td>
<td>32.5</td>
<td>0.87</td>
</tr>
<tr>
<td>Non-Insulin Dependent (%)</td>
<td>66.3</td>
<td>67.5</td>
<td>0.87</td>
</tr>
<tr>
<td>Hyperlipidemia (%)</td>
<td>61.3</td>
<td>61.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>66.3</td>
<td>66.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>50.0</td>
<td>45.0</td>
<td>0.44</td>
</tr>
<tr>
<td>Previous MI (%)</td>
<td>42.5</td>
<td>31.3</td>
<td>0.14</td>
</tr>
<tr>
<td>Multi-vessel Disease (%)</td>
<td>68.8</td>
<td>61.3</td>
<td>0.32</td>
</tr>
<tr>
<td>Hemoglobin A₁c (%)</td>
<td>7.3 ± 1.4</td>
<td>7.4 ± 1.5</td>
<td>0.65</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>63.8 ± 13</td>
<td>66.9 ± 13</td>
<td>0.13</td>
</tr>
</tbody>
</table>

Late Loss at 270 Days (NIDDM and IDDM)

NIDDM patients

- BMS Group (n = 68)
- SES Group (n = 73)

<table>
<thead>
<tr>
<th>In-Segment</th>
<th>In-Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.42 ± 0.4</td>
<td>0.09 ± 0.5</td>
</tr>
<tr>
<td>0.61 ± 0.5</td>
<td>0.1 ± 0.1</td>
</tr>
</tbody>
</table>

P < 0.001

IDDM patients

- BMS Group (n = 33)
- SES Group (n = 30)

<table>
<thead>
<tr>
<th>In-Segment</th>
<th>In-Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.56 ± 0.6</td>
<td>-0.02 ± 0.3</td>
</tr>
<tr>
<td>0.78 ± 0.5</td>
<td>0.05 ± 0.3</td>
</tr>
</tbody>
</table>

P < 0.001

Sabaté M., et al., Circulation 2005; 112: 2175-83
Binary Restenosis at 270 Days (NIDDM and IDDM)

NIDDM patients

In-Segment

P = 0.001

BMS Group (n = 68) SES Group (n = 73)

29.0

8.2

27.5

2.7

IDDM patients

In-Segment

P = 0.002

BMS Group (n = 33) SES Group (n = 30)

43.8

6.7

40.6

6.7

Sabaté M., et al., Circulation 2005; 112: 2175-83
**DIABETES**

Subgroup Analysis for 270-Day Rate of In-Segment Restenosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lesions</th>
<th>In-segment restenosis</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SES</td>
<td>BMS</td>
</tr>
<tr>
<td>Overall</td>
<td>204</td>
<td>7.8</td>
<td>33.7</td>
</tr>
<tr>
<td>IDDM</td>
<td>62</td>
<td>6.7</td>
<td>43.8</td>
</tr>
<tr>
<td>NIDDM</td>
<td>142</td>
<td>8.2</td>
<td>29.0</td>
</tr>
<tr>
<td>Male</td>
<td>133</td>
<td>10.0</td>
<td>36.5</td>
</tr>
<tr>
<td>Female</td>
<td>71</td>
<td>3.0</td>
<td>28.9</td>
</tr>
<tr>
<td>LAD</td>
<td>82</td>
<td>7.5</td>
<td>35.3</td>
</tr>
<tr>
<td>Others</td>
<td>122</td>
<td>7.9</td>
<td>33.9</td>
</tr>
<tr>
<td>CTO Yes</td>
<td>27</td>
<td>7.1</td>
<td>76.9</td>
</tr>
<tr>
<td>CTO No</td>
<td>177</td>
<td>7.9</td>
<td>27.3</td>
</tr>
<tr>
<td>Lesion Length</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤20mm</td>
<td>117</td>
<td>6.9</td>
<td>20.3</td>
</tr>
<tr>
<td>&gt;20mm</td>
<td>87</td>
<td>8.9</td>
<td>52.4</td>
</tr>
<tr>
<td>IIb/IIIa Yes</td>
<td>127</td>
<td>3.0</td>
<td>31.1</td>
</tr>
<tr>
<td>IIb/IIIa No</td>
<td>77</td>
<td>16.2</td>
<td>37.5</td>
</tr>
<tr>
<td>Stent Size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤2.5mm</td>
<td>71</td>
<td>10.5</td>
<td>42.4</td>
</tr>
<tr>
<td>&gt;2.5mm</td>
<td>133</td>
<td>6.2</td>
<td>29.4</td>
</tr>
</tbody>
</table>

TLR at 270 Days

BMS Group (n = 101)  SES Group (n = 103)

P = 0.002  P = 0.004
P < 0.001

TLR, %

31.3  6.3
23.0  5.2
33.3  5.9

All Patients  NIDDM Patients  IDDM Patients

Sabaté M., et al., Circulation 2005; 112: 2175-83
Between April 2003 and May 2004, 1,012 patients with symptomatic coronary artery disease and the presence of ≥ 1 lesion with a diameter stenosis of ≥ 50% RVD: 2.25 mm - 4.0 mm. No limit on # of treated lesions and vessels or lesion length.

1:1 Randomization

Sirolimus-eluting Stent (SES)

n=503

Paclitaxel-eluting stent (PES)

n=509

Prespecified Primary Endpoint (Intention-to-Treat Analysis):
Composite of cardiac death, myocardial infarction (MI), and or ischemia-driven target lesion revascularization (TLR)* at 9 months

* ≥ 50% diameter stenosis with ischemic signs or symptoms OR
≥ 70% diameter stenosis in the absence of ischemic symptoms

SIRTAX: 9-Month Outcomes

<table>
<thead>
<tr>
<th></th>
<th>SES (n=503)</th>
<th>PES (n=509)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Death, MI, or ischemia-driven TLR</td>
<td>6.2%</td>
<td>10.8%</td>
</tr>
<tr>
<td>Prespecified 1° Endpoint</td>
<td>P = 0.009</td>
<td></td>
</tr>
<tr>
<td>Cardiac Death, MI, or clinically-driven TLR</td>
<td>5.8%</td>
<td>9.6%</td>
</tr>
<tr>
<td>Post-hoc 1° Endpoint</td>
<td>P = 0.02</td>
<td></td>
</tr>
</tbody>
</table>

SIRTAX: Pre-Specified Subgroup Analysis of Primary Endpoint (MACE at 9 months)

All Patients (n = 1,012)

Diabetes (n = 201)

No Diabetes (n = 811)

ACS (n = 520)

No ACS (n = 492)

Test for interaction:
- Diabetes: p = 0.13
- ACS: p = 0.05

Between June 11, 2003 and March 15, 2004, 250 patients with diabetes mellitus and coronary artery disease, and with clinically significant angiographic stenosis in a native coronary vessel were enrolled.

1:1 Randomization

- Sirolimus-eluting Stent (SES) n=125
- Paclitaxel-eluting stent (PES) n=125

1° EP: Late lumen loss at 6 months (in-segment analysis)

2° EP: Angiographic restenosis at 6 months ≥ 50% diameter stenosis (in-segment analysis)
Target lesion revascularization at 9 months

**Primary Endpoint:**
In-Segment Late Lumen Loss

**Non-inferiority margin of late loss (0.16 mm)**

0.24 mm
95% CI (0.09 to 0.39)

P = 0.002*

* After adjustment for baseline differences, the result remained significant (p = 0.0001)

Late Luminal Loss at Follow-Up

<table>
<thead>
<tr>
<th></th>
<th>SES (n = 102)</th>
<th>PES (n = 103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal Margin</td>
<td>0.06 ± 0.57</td>
<td>0.26 ± 0.70</td>
</tr>
<tr>
<td>In-Stent Margin</td>
<td>0.19 ± 0.44</td>
<td>0.46 ± 0.64</td>
</tr>
<tr>
<td>Distal Margin</td>
<td>0.28 ± 0.46</td>
<td>0.49 ± 0.58</td>
</tr>
<tr>
<td>In-Segment</td>
<td>0.43 ± 0.45</td>
<td>0.62 ± 0.67</td>
</tr>
</tbody>
</table>

*P-values after adjustment for baseline characteristics

In-Segment Late Luminal Loss by Diabetic Status

<table>
<thead>
<tr>
<th></th>
<th>SES</th>
<th>PES</th>
</tr>
</thead>
<tbody>
<tr>
<td>IDDM</td>
<td>0.41 ± 0.42</td>
<td>0.44 ± 0.46</td>
</tr>
<tr>
<td>NIDDM</td>
<td>0.72 ± 0.66</td>
<td>0.65 ± 0.60</td>
</tr>
<tr>
<td>All Patients</td>
<td>0.43 ± 0.45</td>
<td>0.67 ± 0.62</td>
</tr>
</tbody>
</table>

P = 0.02 (P = 0.001*)

* P-values after adjustment for baseline characteristics

All-cause Mortality in Pooled Analysis

RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS

Total population
N=1748

Diabetic patients
N=428

Non-diabetic patients
N=1318

<table>
<thead>
<tr>
<th></th>
<th>BMS</th>
<th>SES</th>
<th>0</th>
<th>360</th>
<th>720</th>
<th>1080</th>
<th>1440</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS</td>
<td>869</td>
<td>877</td>
<td>855</td>
<td>860</td>
<td>835</td>
<td>838</td>
<td>816</td>
</tr>
<tr>
<td>SES</td>
<td>869</td>
<td>877</td>
<td>855</td>
<td>860</td>
<td>835</td>
<td>838</td>
<td>816</td>
</tr>
</tbody>
</table>

Logrank P-value: 0.27

Logrank P-value: 0.004

Logrank P-value: 0.59

Spaulding C et al. NEJM 2007;356:989-97
Intravascular Ultrasound (IVUS): Volumetric Analysis

DES in Complex Lesions

- Diabetes
- Long lesions
- Small vessels
- Left main
- Multivessel disease
Long-DES I Registry in Korea

From March 2003 - February 2004

De-novo Lesions
(≥ 24mm)

637 patients - 739 lesions

CYPHER
(≥ 28mm)

294 patients
344 lesions

TAXUS
(≥ 28mm)

166 patients
194 lesions

Bare Metal
(≥ 28mm)

177 patients
201 lesions

Restenosis Rate of Long-DES I

In-segment:
- Cypher: 7.4% (20/271)
- Taxus: 21.3% (32/150)
- BMS: 42.5% (68/160)

In-stent:
- Cypher: 6.3% (17/271)
- Taxus: 16.0% (24/150)
- BMS: 40.6% (65/160)

P-values:
- In-segment: P<0.001
- In-stent: P<0.001

Preliminary Analysis

Long coronary lesions (>25mm) requiring single or multiple DES (planned total stent length ≥32mm)

1:1 randomization

SES (250 patients)

168 patients (76.3%) of eligible patients

Clinical F/U at 9 months

200 patients (80%) of study population

PES (250 patients)

164 patients (75.2%) of eligible patients

Angiographic F/U at 6 months

206 patients (82%) of study population

ACC 2006; Oral Presentation.
Angiographic Restenosis at 9-Month Follow-up

P = 0.007
P = 0.010
P = 0.165
P = 0.113

ACC 2006; Oral Presentation.
Clinical Outcomes at 9-Month Follow-up

<table>
<thead>
<tr>
<th></th>
<th>SES</th>
<th>PES</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>200</td>
<td>206</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1 (1.0%)</td>
<td>0</td>
<td>0.493</td>
</tr>
<tr>
<td>Death: Cardiac</td>
<td>1 (1.0%)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Death: Non-cardiac</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>2 (1.0%)*</td>
<td>0</td>
<td>0.242</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>2 (1.0%)</td>
<td>0</td>
<td>0.242</td>
</tr>
<tr>
<td>Stent thrombosis: Acute</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Stent thrombosis: Subacute</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Stent thrombosis: Late</td>
<td>1**</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>TLR</td>
<td>5 (2.5%)</td>
<td>16 (7.8%)</td>
<td>0.014</td>
</tr>
<tr>
<td>MACE</td>
<td>6 (3.0%)</td>
<td>16 (7.8%)</td>
<td>0.027</td>
</tr>
</tbody>
</table>

* Both of them were related to subacute and late stent thrombosis
** This patient presented with STEMI and cardiogenic shock 3 months after the index procedure. This patient died before emergent revascularization

ACC 2006; Oral Presentation.
DES in Complex Lesions

- Diabetes
- Long lesions
- Small vessels
- Left main
- Multivessel disease
In-Lesion Restenosis by Vessel Size

<table>
<thead>
<tr>
<th>Baseline Reference Vessel Diameter</th>
<th>Bare Metal Stent</th>
<th>SES</th>
<th>p &lt; 0.001 for all</th>
</tr>
</thead>
<tbody>
<tr>
<td>~ 2.3 mm</td>
<td>42.9%</td>
<td>18.6%</td>
<td></td>
</tr>
<tr>
<td>~ 2.8 mm</td>
<td>36.5%</td>
<td>6.3%</td>
<td></td>
</tr>
<tr>
<td>~ 3.3 mm</td>
<td>30.2%</td>
<td>1.9%</td>
<td></td>
</tr>
</tbody>
</table>

8-Month Late Loss

- SIRIUS – Bare Metal Stent (n=213)
- SIRIUS - SES (n=232)
- SVELTE - SES (n=95)

Late Loss (mm)

Proximal: 0.36, 0.19, 0.18
In-Stent: 0.97, 0.16, 0.22
Distal: 0.23, 0.04, 0.13

Clinical Outcomes at 8 Months

- SIRIUS – Bare Metal Stent (n=323)
- SIRIUS - SES (n=350)
- SVELTE - SES (n=101)

<table>
<thead>
<tr>
<th>Event</th>
<th>SIRIUS – Bare Metal Stent</th>
<th>SIRIUS - SES</th>
<th>SVELTE - SES</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>0.9</td>
<td>0.9</td>
<td>2.0</td>
<td>NS</td>
</tr>
<tr>
<td>MI</td>
<td>2.8</td>
<td>3.1</td>
<td>3.0</td>
<td>NS</td>
</tr>
<tr>
<td>TLR</td>
<td>12.7</td>
<td>4.6</td>
<td>0.0</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

8-Month Clinical Outcomes

- **Bare Metal Stent (n = 128)**
  - Death: 1.6 (p = 0.24)
  - MI: 7.8 (p = 0.04)
  - TLR: 21.1 (p = 0.002)
  - Stent Thrombosis: 3.1 (p = 0.21)

- **SES (n = 129)**
  - Death: 0.0
  - MI: 1.6
  - TLR: 7.0
  - Stent Thrombosis: 0.8

In-Segment Binary Restenosis and Late Loss at 8-Month Follow-Up

### In-Segment Binary Restenosis Primary Endpoint
- **Bare Metal Stent**: 53.1%
- **SES**: 9.8%
  - **Change**: 82%, *P < 0.001*

### In- Segment Late Loss
- **Bare Metal Stent**: 0.69 mm
- **SES**: 0.16 mm
  - **Change**: 77%, *P < 0.001*

Summary of Angiographic Findings at 8-Month Follow-up (In-Lesion)

**SES (n=239)**

- MLD: 1.70 ± 0.426
- Late Loss: 0.18 ± 0.435

**P < 0.0001**

**Bare-Metal Stent (n=214)**

- MLD: 1.13 ± 0.603
- Late Loss: 0.75 ± 0.621

- % DS: 26.8 ± 15.02
- BAR (%): 8.7

**P < 0.0001**

Bachinsky WB, TCT 2006; Oral Presentation.
MACE, TVF, and TVR at 1-Year

- **SES (n=239)**
  - TVF: 8.3%
  - TVR: 6.7%
  - MACE: 8.3%

- **Bare-Metal Stent (n=214)**
  - TVF: 29.5%
  - TVR: 28.6%
  - MACE: 29.0%

*P* < 0.0001 for all comparisons.

Bachinsky WB, TCT 2006; Oral Presentation.
Stent Thrombosis (Protocol Definition) Through 1-Year

P = NS for all

2.1% 1.9%

SES (n = 239) BMS (n = 214)

Bachinsky WB, TCT 2006; Oral Presentation.
Stent Thrombosis Using Dublin Definition Through 1-Year (Only RAVEL, SIRIUS, C-SIRIUS, & E-SIRIUS)

P = NS for all

% of Patients

- Late ST (> 30d, < 1y)
- Early ST (< 30d)

SES (n = 170)
BMS (n = 179)

1.2%
1.7%

1.2
0.6
1.2
Late Loss associated in Small Vessel Subgroups

Small Vessels May Need Specific Product Designs
The CardioMind Sparrow™: Stent on a .014” Guide Wire Platform
<table>
<thead>
<tr>
<th>The CardioMind Sparrow™</th>
<th>Coronary Stent Delivery System</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>.014” Guidewire Based</strong></td>
<td>Delivery System</td>
</tr>
<tr>
<td><strong>Nitinol Stent</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Drug in Biodegradable</strong></td>
<td>Coating</td>
</tr>
</tbody>
</table>

- Sirolimus and Polymer
- RO Coating
- Stent
CARE II – CardioMind Sirolimus DES Study -**Preliminary**

2:1 CardiMind DES to CardioMind Bare Metal

(200 patients planned enrollment)

Single De Novo Native Coronary Artery Lesions (Type A-B2)

2 Vessel (Target and Non-Target Vessel) Treatment allowed

- Vessel Diameters: 2.0 – 2.75 mm
- Stent Diameters: 2.5 – 3.5 mm
- Lesion Length: ≤ 20 mm
- Primary Stent Length: 22 mm
- 12 mm Length for Bailout Only

Pre-Dilatation and Post-Dilatation Required

**Clinical Follow-Up**

<table>
<thead>
<tr>
<th>30d</th>
<th>6mo</th>
<th>9mo</th>
<th>1 yr</th>
<th>2yr</th>
<th>3yr</th>
<th>4yr</th>
<th>5 yr</th>
</tr>
</thead>
</table>

Angiographic / IVUS Follow-Up @ 8 mo

**Primary Endpoint:** In Stent Late lumen loss @ 8 mo

**Key Secondary Endpoints:**

- MACE at 30 days (death, MI and TVR)
- Sub acute thrombosis (SAT)
- Device, Lesion and Procedure Success
- MACE at hospital discharge, 6, 9 & 12 mos
- Clinically driven TLR at 6, 9 & 12 mos
- ABR, LL and % volume obstruction at 8 mos

Anti-Platelet Therapy for 6 months
DES in Complex Lesions

- Diabetes
- Long lesions
- Small vessels
- Left main
- Multivessel disease
### Published Report of DES in UPLM

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>In-hosp Death</th>
<th>MI</th>
<th>1 Year Death</th>
<th>Restenosis</th>
<th>TVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>deLezo '04</td>
<td>52</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Arampatzis '04</td>
<td>16</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Agonstoni '05</td>
<td>58</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Chieffo '05</td>
<td>85</td>
<td>0</td>
<td>6</td>
<td>3.5</td>
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<td>19</td>
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<td>Valgimigli '05</td>
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<td>11</td>
<td>4</td>
<td>14</td>
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<tr>
<td>Park '05</td>
<td>102</td>
<td>0</td>
<td>6.9</td>
<td>0</td>
<td>6</td>
<td>2</td>
</tr>
</tbody>
</table>

Sum:

- Total N: 816
- In-hosp Death: 0.011%
- MI: 4.7%
- 1 Year Death: 0.14%
- Restenosis: 6.19%
- TVR: 2.19%
# Brief Reports of DES in UPLM

<table>
<thead>
<tr>
<th>Abstract ’04-’05</th>
<th>N</th>
<th>IH Death</th>
<th>FU (mo)</th>
<th>Death</th>
<th>TVR</th>
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<tbody>
<tr>
<td>Nakamura</td>
<td>138</td>
<td>0</td>
<td>12</td>
<td>0</td>
<td>3</td>
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<tr>
<td>Buszman</td>
<td>124</td>
<td>2.4</td>
<td>17</td>
<td>5.6</td>
<td>20</td>
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<td>Chieffo</td>
<td>105</td>
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<td>15.2</td>
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<tr>
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<td>6</td>
<td>4</td>
<td>2</td>
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<tr>
<td>DiSalvo</td>
<td>80</td>
<td>3.7</td>
<td>6</td>
<td>4.2</td>
<td>4.2</td>
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<tr>
<td>Sheiban</td>
<td>86</td>
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<td>12</td>
<td>4.6</td>
<td>16</td>
</tr>
<tr>
<td>Price</td>
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<td>0</td>
<td>3</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>Lefevre</td>
<td>241</td>
<td>1</td>
<td>7</td>
<td>4.2</td>
<td>5.2</td>
</tr>
<tr>
<td>Pinto</td>
<td>83</td>
<td>1.2</td>
<td>6</td>
<td>3.6</td>
<td>7</td>
</tr>
<tr>
<td>Gerot</td>
<td>174</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total</th>
<th>1,128</th>
<th>0-4%</th>
<th>0-7%</th>
<th>2-30%</th>
</tr>
</thead>
</table>
Very low clinical event rates at 6 months

Cypher in 221 Pts

- Death: 1.8%
- MI: 0.6%
- TLR: 1.8%
- MACE: 3.7%
DES vs. BMS in Milan

Six-month clinical and angiographic follow-up

- **Cardiac death**
  - BMS: 9.3%
  - DES: 3.5%
  - $P=0.17$

- **Restenosis**
  - BMS: 30.6%
  - DES: 18.8%
  - $P=0.18$

- **TLR**
  - BMS: 30.6%
  - DES: 18.8%
  - $P=0.11$

- **MACE**
  - BMS: 42.1%
  - DES: 24.7%
  - $P=0.03$

Chieffo A et al. Circulation 2005;111:791
LM Stenting: Overall Restenosis - 7.9 %

P = 0.003

P = NS

P = 0.002

Park SJ et al, J Am Coll Cardiol 2005;45:351
DES in Complex Lesions

- Diabetes
- Long lesions
- Small vessels
- Left main
- Multivessel disease
ARTS II: 3-Year Follow-up

607 patients

18 death

1,080 Days Follow-up

589 Alive

414 Seen at outpatient clinic with ECG

175 Not seen at outpatient clinic

Withdrawal 3/175
Lost to FUP 2/175
Death >1080days** 2/175

• Phone contact patient 140/168
  • By GP 9/168
  • By relative 2/168
  • Other 17/168

ECG obtained* 132/168
No ECG obtained 36/168

* ECG obtained by center
** Died at 1087 and 1116 days

Serruys PW., et al., ACC 2007; Oral Presentation.
ARTS II: Mortality Through 3 Years*

Survival (%)

Time (Months)

P (log rank) = 0.20 between ARTS II and ARTS I-CABG

P (log rank) = 0.33 between ARTS II and ARTS I-PCI

Serruys PW., et al., ACC 2007; Oral Presentation.
**ARTS II**

**ARTS II: Death, Cerebrovascular Accidents, and MI’s Through 3 Years***

- ARTS II
- ARTS I CABG
- ARTS I PCI

P (log rank) = 0.07 between ARTS II and ARTS I-CABG

P (log rank) = 0.004 between ARTS II and ARTS I-PCI

Serruys PW., et al., ACC 2007; Oral Presentation.
ARTS II

ARTS II: Reintervention Through 3 Years*

P (log rank) <0.001 between ARTS II and ARTS I-CABG

93.4%

P (log rank) <0.001 between ARTS II and ARTS I-PCI

85.5%

73.3%

Serruys PW., et al., ACC 2007; Oral Presentation.
ARTS II: MACCE Through 3 Years*

- ARTS II
- ARTS I CABG
- ARTS I PCI

P (log rank) = 0.22 between ARTS II and ARTS I-CABG

P (log rank) <0.001 between ARTS II and ARTS I-PCI

Serruys PW., et al., ACC 2007; Oral Presentation.
* Re-adjudication according to Dublin definitions
- **Definite (angiography pathological confirmation)**
- **Definite & Probable (MI in stent area)**
- **Definite, probable and possible (any unexplained death)**

Serruys PW., et al., ACC 2007; Oral Presentation.
All patients with Left main and/or 3-Vessel Disease

Minimal In- or Exclusion Criteria

Local Heart team (Interventional Cardiologist & Cardiothoracic Surgeon)

eligible for both treatment options

Randomized Trial

CABG (n=900)

TAXUS® Stent (n=900)

Nested Registries

CABG

TAXUS® Stent
Which stent is better for complex lesions?
# Included SES vs. PES Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Total No. of patient</th>
<th>Mean Clinical FU in months</th>
<th>Special notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASKET</td>
<td>545</td>
<td>18.2</td>
<td></td>
</tr>
<tr>
<td>CORPAL</td>
<td>652</td>
<td>30.5</td>
<td></td>
</tr>
<tr>
<td>ISAR-DESIRE</td>
<td>200</td>
<td>33.9</td>
<td>Bare metal in-stent restenosis</td>
</tr>
<tr>
<td>ISAR-DIABETES</td>
<td>250</td>
<td>32.1</td>
<td>Diabetic patients</td>
</tr>
<tr>
<td>ISAR-SMART 3</td>
<td>360</td>
<td>33.9</td>
<td>Small vessels, no diabetics</td>
</tr>
<tr>
<td>LONGDES II</td>
<td>500</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>PROSIT</td>
<td>308</td>
<td>12.0</td>
<td>Acute myocardial infarction</td>
</tr>
<tr>
<td>REALITY</td>
<td>1353</td>
<td>24.1</td>
<td></td>
</tr>
<tr>
<td>SIRTAX</td>
<td>1012</td>
<td>24.2</td>
<td></td>
</tr>
<tr>
<td>SORT-OUT II</td>
<td>2098</td>
<td>9.0</td>
<td></td>
</tr>
<tr>
<td>TAXI</td>
<td>202</td>
<td>36.9</td>
<td></td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>7480</strong></td>
<td><strong>20.0</strong></td>
<td></td>
</tr>
</tbody>
</table>
## Risk of MACE

### No. of events / Total No. of patients

<table>
<thead>
<tr>
<th>Trial</th>
<th>SES group</th>
<th>PES group</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASKET</td>
<td>32/264</td>
<td>35/281</td>
</tr>
<tr>
<td>CORPAL</td>
<td>51/331</td>
<td>52/321</td>
</tr>
<tr>
<td>ISAR-DESIRE</td>
<td>23/100</td>
<td>37/100</td>
</tr>
<tr>
<td>ISAR-DIABETES</td>
<td>30/125</td>
<td>30/125</td>
</tr>
<tr>
<td>ISAR-SMART 3</td>
<td>34/180</td>
<td>47/180</td>
</tr>
<tr>
<td>LONG-DES II</td>
<td>27/250</td>
<td>42/250</td>
</tr>
<tr>
<td>PROSIT</td>
<td>9/154</td>
<td>18/154</td>
</tr>
<tr>
<td>REALITY</td>
<td>93/684</td>
<td>104/669</td>
</tr>
<tr>
<td>SIRTAX</td>
<td>57/503</td>
<td>87/509</td>
</tr>
<tr>
<td>SORT-OUT II</td>
<td>83/1065</td>
<td>89/1033</td>
</tr>
<tr>
<td>TAXI</td>
<td>14/102</td>
<td>9/100</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td><strong>453/3758</strong></td>
<td><strong>550/3722</strong></td>
</tr>
</tbody>
</table>

### Hazard Ratio

- **Hazard Ratio**: 0.79 (0.69, 0.91)

**Test for Heterogeneity**: Cochran $Q = 12.2$ (d.f. = 10) $P = .27$

**Test for Inconsistency**: $I^2 = 18.2\%$
Target Lesion Revascularization (TLR) Rates Differ in DES Comparison RCTs

TLR rates for 7 RCTs Demonstrate Correlation between Taxus and CYPHER

TLR rates increased 3.5x faster with Taxus than with Cypher

R^2 = 0.85

Conclusions

- No significant difference in mortality.
- A significantly lower risk of stent thrombosis.
- A trend toward a lower combined risk of death or myocardial infarction.
- A significantly lower risk of death, myocardial infarction or reintervention.

Compared with Taxus stent, Cypher stent is associated with:
## Risk of Stent Thrombosis

<table>
<thead>
<tr>
<th>Trial</th>
<th>SES group</th>
<th>PES group</th>
<th>Favors SES</th>
<th>Favors PES</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASKET</td>
<td>4/264</td>
<td>5/281</td>
<td></td>
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</tr>
<tr>
<td>CORPAL</td>
<td>2/331</td>
<td>4/321</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISAR-DESIRE</td>
<td>0/100</td>
<td>2/100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISAR-DIABETES</td>
<td>0/125</td>
<td>2/125</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ISAR-SMART 3</td>
<td>1/180</td>
<td>1/180</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LONG-DES II</td>
<td>1/250</td>
<td>5/250</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROSIT</td>
<td>0/154</td>
<td>2/154</td>
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<tr>
<td>REALITY</td>
<td>6/684</td>
<td>18/669</td>
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<tr>
<td>SORT-OUT II</td>
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<tr>
<td>TAXI</td>
<td>2/102</td>
<td>2/100</td>
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<tr>
<td><strong>Overall</strong></td>
<td>28/2693</td>
<td>56/2689</td>
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</tbody>
</table>

Hazard Ratio: 0.54 (0.34, 0.85)

Test for Heterogeneity: Cochran Q=5.3 (d.f.=9) P=.81
Test for Inconsistency: $I^2 = 0.0\%$
Risk of Death or MI

<table>
<thead>
<tr>
<th>Trial</th>
<th>SES group</th>
<th>PES group</th>
<th>Favors SES</th>
<th>Favors PES</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASKET</td>
<td>23/264</td>
<td>29/281</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CORPAL</td>
<td>33/331</td>
<td>37/321</td>
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</tr>
<tr>
<td>ISAR-DIABETES</td>
<td>26/125</td>
<td>26/125</td>
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<td></td>
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<tr>
<td>ISAR-DESIRE</td>
<td>11/100</td>
<td>10/100</td>
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<td></td>
</tr>
<tr>
<td>ISAR-SMART 3</td>
<td>19/180</td>
<td>19/180</td>
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<td></td>
</tr>
<tr>
<td>LONG-DES II</td>
<td>22/250</td>
<td>27/250</td>
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<tr>
<td>REALITY</td>
<td>54/684</td>
<td>69/669</td>
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<tr>
<td>SIRTAX</td>
<td>41/503</td>
<td>46/509</td>
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<tr>
<td>TAXI</td>
<td>11/102</td>
<td>10/100</td>
<td></td>
<td></td>
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<tr>
<td><strong>Overall</strong></td>
<td><strong>240/2539</strong></td>
<td><strong>273/2535</strong></td>
<td><strong>0.86 (0.72, 1.02)</strong></td>
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</table>

Test for Heterogeneity: Cochran Q=1.2 (d.f.=8) P=.99
Test for Inconsistency: $I^2$ =0.0%