The Drug Eluting Stent
Firestorm

Christian Spaulding
Cardiology Department
Cochin Hospital, Paris Descartes University,
Paris, France
What are we talking about?

Atherosclerotic coronary artery lesions
Percutaneous Coronary Intervention (PCI)
Restenosis: 10-30%

Three months after….

Smooth muscle cell proliferation
Drug-Eluting Stents Reduce Restenosis

Metal stent

Polymer

Anti-proliferative drug

![Graph](chart.png)
Interventional Cardiology
Before 09/06

- Drastic reduction in restenosis rates
- Increase in number of PCI procedures
- Rate of late stent thrombosis at one year: 0.3 to 0.6%, similar to bare metal stents
Incomplete Neointimal Coverage of Sirolimus-Eluting Stents

Kotani J et al. JACC 2006;47:2108

Sirolimus-Eluting Stent (N=15) vs. Bare Metal Stents (N=22)

- Incomplete Neointimal Coverage:
  - Sirolimus-Eluting Stent: Grade 0=20%, Grade 1=0%
  - Bare Metal Stents: Grade 0=0%, Grade 1=6.7%

- Complete Neointimal Coverage:
  - Sirolimus-Eluting Stent: Grade 2=0%, Grade 3=6.7%
  - Bare Metal Stents: Grade 2=13.3%, Grade 3=6.7%

P < 0.001
And the Firestorm Begins..

2007 Oscar of the most viewed slide during cardiology meetings!

Do drug-eluting stents increase deaths?
All randomized studies up to latest available follow-up

Rate of death or Q-MI (%)

<table>
<thead>
<tr>
<th>Group</th>
<th>Rate</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>SES Control (BMS)</td>
<td>3.9</td>
<td>870</td>
</tr>
<tr>
<td>SES DES</td>
<td>6.3</td>
<td>878</td>
</tr>
<tr>
<td>p=0.03</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>Rate</th>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>PES Control (BMS)</td>
<td>2.3</td>
<td>1675</td>
</tr>
<tr>
<td>PES DES</td>
<td>2.6</td>
<td>1685</td>
</tr>
<tr>
<td>p=0.68</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Consequences and Actions

- Sharp drop in DES implantation rate in the US and in some countries in Europe
- FDA panel meeting in December 06
- New England Journal of Medicine: early release of several manuscripts on DES on February 13, 2007
A Pooled Analysis of Data Comparing Sirolimus-Eluting Stents with Bare-Metal Stents

No significant difference between groups
Diverging curves
No difference in all-MI

Safety and Efficacy of Sirolimus and Paclitaxel-Eluting Coronary Stents

Analysis of 14 Trials Comparing Sirolimus-Eluting Stents with Bare-Metal Stents

Click Swiss on the net....
MACE rates individual data (pooled data HCRI & Cardialysis) vs. Camenzind

<table>
<thead>
<tr>
<th>RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS</th>
<th>Camenzind</th>
<th>Real data to 1440 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cypher</td>
<td>Control</td>
</tr>
<tr>
<td>N = 1748</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death total</td>
<td>4.7%</td>
<td>3.3%</td>
</tr>
<tr>
<td>Q-MI</td>
<td>1.6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Non-Q-MI</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Death total and Q-MI</td>
<td>6.3%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Death total and all MI</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Independent physician-directed meta-analysis versus Independent physician-assessed patient level meta-analysis
Early and Late Coronary Stent Thrombosis of Drug-Eluting Stents in Routine Clinical Practice

Between 30 days to 3 years:
Slope = 0.6% / year

N=8,146 Patients

The Ontario Registry

Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis


Lancet, 2007; 370: 937-48
Target Lesion Revascularization
DES vs BMS

Cumulative incidence of target lesion revascularisation (%)

SES vs BMS: HR 0.30 (95%-CI 0.24-0.37, p<0.0001)
PES vs BMS: HR 0.42 (95%-CI 0.33-0.53, p<0.0001)
SES vs PES: HR 0.70 (95%-CI 0.56-0.84, p=0.0021)

<table>
<thead>
<tr>
<th>N of events/patients</th>
<th>Years after Initial procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS</td>
<td>4763</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>PES</td>
<td>6328</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>SES</td>
<td>6621</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
While the DES firestorm demonstrated the danger of excessive media coverage of « hotline » sessions, it also was a wake-up call for more careful evaluation of new techniques.

Changes in clinical practice must be based solely on data published in peer reviewed manuscripts.
Get the right data before making a decision....
Back-up
DES Registration in France (2009)

- For a new DES:
  - Sufficient pre-clinical data
  - A non-inferiority study comparing the new stent to a DES already registered (350-400 pts)
  - A randomized study or a registry focused on safety (1200-1500 pts)
  - Data is reviewed by a panel with interventional cardiologists, methodologists, etc...
PCI in France: Regulations

- European and French Society of Cardiology Recommendations
- Law with the minimal number of PCIs (> 400 per year)
- Greater Paris Area Registry