PCI / Stents: devices and techniques

New stent platforms

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DES Generations

1st Generation

Cypher - Taxus

2nd Generation

a) Thin struts, thin permanent polymer

b) Bioabsorbable polymer

c) No polymer
### Drug-Eluting Stents Problems!

- **Late loss = 0**
- **7 years**
- **Delayed Healing!**

#### Late stent thrombosis
- **40 mos**

#### Angioscopy
- **BMS**
- **DES**

#### Inflammation
- **Giant cells**
- **Eos**

#### Abnormal Vasomotion

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Sirolimus</td>
<td>Control</td>
<td></td>
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</tr>
</tbody>
</table>

*P<0.001 vs. control*

#### IVUS
- **Incomplete apposition**
XIENCE V*: Design Parameters and Pre-clinical Results

- Low profile, flexible, deliverable stent
- Highly resistant to strut fracture
- Thin, adhesive, inert durable polymer
  - promotes functional endothelialization
  - minimal bonding and webbing
  - no significant inflammation or hypersensitivity reaction
  - fluoropassivation resists platelet, WBC and thrombus deposition
- Lowest dose of a “limus” on any DES

*AKA Promus
SPIRIT IV Study Algorithm

3690 pts enrolled at 66 U.S. sites

Randomized 2:1 XIENCE V®:TAXUS® Express²
Stratified by diabetes and presence of complex lesions
Pre-dilatation mandatory

Everolimus-eluting
XIENCE V

Paclitaxel-eluting
TAXUS

Aspirin ≥80 mg QD for 5 years; clopidogrel 75mg QD for at least 12 mos (if not at high risk for bleeding)

Clinical f/u only: 1, 6, 9 months and yearly for 1-5 years
SPIRIT IV: TLR Through 1 Year

Ischemia-driven TLR (%)

- **XIENCE V** (n=2458)
  - Number at risk: 2458, 2419, 2392, 2353, 2328

- **TAXUS Express** (n=1229)
  - Number at risk: 1229, 1185, 1158, 1140, 1125

HR [95%CI] = 0.54 [0.38, 0.78]

p = 0.0008

Δ 2.2%

SPIRIT IV: Stent Thrombosis

STMN1 Definite or Probable

XIENCE V (n=2458)

TAXUS Express (n=1229)

HR [95%CI] = 0.27 [0.11, 0.67]
p = 0.003

Δ 0.77%

0.29%

1.06%

Stent thrombosis (%)

ARC Definite or Probable

Months

Number at risk

XIENCE V  2458  2426  2412  2388  2376

TAXUS  1229  1195  1184  1174  1166

COMPARE Trial (n=1800)

- AMI 25%
- Left main 2%
- Chronic renal failure 3%
- Calcification 34%
- Direct stenting 34%
- Bifurcation 10%
- Multistenting 62%
- Diabetes 18%
- Ostial 19%
- Saphenous graft 2%
- Thrombus 24%
- Multivessel 27%
- NSTEMI 23%
- CTO 4%
- Kedhi et al. Lancet 2010 on-line
Connections/bridges between hoops play a major role in flexibility.
The number of connections controls cell size and flexibility.

Bridges/connectors link hoops

Welds link hoops

- **Cypher™**: 0.0055” Stainless Steel
- **Express™**: 0.0052” Stainless Steel
- **Liberté™**: 0.0038” Cobalt Chromium
- **Driver™**: 0.0036” Platinum Chromium
- **Multi-Link Vision™**: 0.0032” Platinum Chromium
- **Element™**: 0.0032” Platinum Chromium
Some observations with the Element Stent

1. Zig zag hoops with 2 straight diagonal bridges
2. Platinum Chromium
3. Everolimus and proven polymer
4. Thin strut 81microns
5. Radio-opacity is greater than CoCr or stainless steel

Ormiston PCR 2010
Platinum Chromium (Element Stent)

Platinum*: 33%
Chromium: 18%
Nickel: 9%
Iron: 37%
Molybdenum: 2.6%
Manganese: 0.05%

*Platinum fully incorporated in the alloy (not coating)
Two Drug Strategy

Paclitaxel
Element Stent
Trial Complete
N=1488

Everolimus
Element Stent
Trial Complete
N=1828
Element SV (2.25)

Element SWH (2.50, 2.75)

Element WH (3.00, 3.50)

Element LV (4.00, 4.50)

Element Stent Designs
Acute Stent Recoil for 3mm diam Stents (n=5 for each stent)

Recoil is related to metal, design and strut thickness

- Cobalt Chromium
- Stainless Steel
- Platinum Chromium
Drug-eluting Stents “3rd Generation”

Resolute

Zotarolimus Drug

BioLinx Polymer

Driver Stent

Regent

Biomatrix

Hydrophilic

Hydrophobic

Biomatrix

Biolimus A9

PLLA

Vision
BioLinx Polymer in vivo Elution

Greater than 85% of the drug is eluted at 60 days
Complete drug content exhausted by 180 days

Carter et al TCT 2006
RESOLUTE All Comers

Co-Pls: Profs. Serruys, Silber, Windecker

Enrollment Complete

Real World (Open Label)
All Comers with symptomatic coronary artery disease

Resolute Stent
n ≈ 1,150

Control Xience V Stent
n ≈ 1,150

Clinical Endpoints

Clinical/MACE

Angio/IVUS

Primary Endpoint: Composite – Cardiac Death, Target Vessel MI, TLR @ 12mo
Secondary Endpoints: Composite @ 30d, 6mo, 2 – 5 yr; angiographic & optical coherence tomography (OCT) parameters @ 13 mo
Drug Therapy: ASA and clopidogrel/ticlid ≥ 6 months (per guidelines)
RESOLUTE All-Comers

2,292 unselected patients randomized 1:1 to RESOLUTE vs. XIENCE V

- **TLF 12 months**
  - XIENCE V: 8.2%
  - RESOLUTE: 8.3%
  - **P=0.94**

- **Definite ST 12 months**
  - XIENCE V: 0.3%
  - RESOLUTE: 1.2%
  - **P=0.01**

- **In segment late loss (mm) 13 months**
  - XIENCE V: 0.06 ± 0.40
  - RESOLUTE: 0.15 ± 0.43
  - **P=0.04**

Serruys PW et al. NEJM 2010.
**Biodegradable Drug Carrier:**

- Stainless steel stent platform, 112 μm strut thickness with a quadrature link design
- Biolimus A9 – 10x more lipophilic than sirolimus, with similar potency
- Biolimus A9 / Poly L-Lactic Acid) 50:50 mix; 10 microns coating thickness
- Abluminal coating
- Degrades in 9 months into CO$_2$ + H$_2$O

**BioMatrix Stent Platform**

**Bioabsorbable Polymer DES**
Superior Strut Coverage and Stent Apposition

Lesions with at least 5% uncovered struts

- BioMatrix Flex™ (n=26), n strut = 6476
- Cypher® Select™ (n=20), n strut = 4592

\[ p = 0.005 \]

Lesions with at least 5% malapposed struts

- BioMatrix Flex™ (n=26), n strut = 6476
- Cypher® Select™ (n=20), n strut = 4592

\[ p = 0.04 \]

Di Mario, C., TCT 2008
Complex Patients - STEMI
12 Month Def/Prob Stent Thrombosis

Probable or Definite ST

$\text{Cypher}$

$\text{BioMatrix}$

$p=0.05$

-57%

Buszman, P., PCR 2009
Interference of Drug-Eluting Stents With Endothelium-Dependent Coronary Vasomotion
Evidence for Device-Specific Responses

Hamilos et al.
**NEVO™ Becomes Polymer-Free in ~90 Days**

**Fully Bioresorbable PLGA Polymer**

- Explants from the porcine coronary artery
- Complete resorption in 3-4 months
- Exclusively housed in the reservoirs
- Fully metabolized
- Highly biocompatible and hemocompatible
- Controlled Sirolimus release without a surface coating
The downside of DES…vessel wall distortion
Incomplete stent apposition detected at the time of stent thrombosis occurring in 124 pts; data presented at PCR 2010 by Petteri Kosonen, MD, of Tempere University Hospital (Tampere, Finland)

<table>
<thead>
<tr>
<th></th>
<th>Acute (&lt; 24 hrs)</th>
<th>Early (24 hrs - 30 d)</th>
<th>Late (30 d – 1 yr)</th>
<th>Very Late(^a) (&gt; 1 yr)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS, n (%)</td>
<td>0 (0)</td>
<td>7 (58%)</td>
<td>0 (0)</td>
<td>3 (16%)</td>
<td>10 (27%)</td>
</tr>
<tr>
<td>DES, n (%)</td>
<td>2 (29%)</td>
<td>4 (31%)</td>
<td>1 (17%)</td>
<td>30 (49%)</td>
<td>37 (43%)</td>
</tr>
</tbody>
</table>

\(^a\) \text{P} = 0.02
# DES with bioabsorbable polymer

<table>
<thead>
<tr>
<th>DES</th>
<th>Stent platform</th>
<th>Drug</th>
<th>Polymer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biomatrix, Biosensors</td>
<td>Stainless steel 137 µm</td>
<td>Biolimus A9 15.6µg/mm</td>
<td>PLA: polylactic acid, abluminal</td>
</tr>
<tr>
<td>Cardiomind, Sparrow, CardioMind</td>
<td>Nitinol self expandable 61 µm</td>
<td>Sirolimus 5.2µg/mm</td>
<td>PLA+PLGA</td>
</tr>
<tr>
<td>ELIXIR-DES, Elixir Medical</td>
<td>Cobalt-chromium 81 µm</td>
<td>Novolimus 5µg/mm</td>
<td>Polyester or polylactide</td>
</tr>
<tr>
<td>JACTAX, Boston Scientific</td>
<td>Stainless steel 96.5 µm</td>
<td>Paclitaxel 0.6µg/mm</td>
<td>D-lactic polylactic acid</td>
</tr>
<tr>
<td>NEVO, Cordis</td>
<td>Cobalt-chromium 99 µm</td>
<td>Sirolimus 7.4µg/mm</td>
<td>Polylactic-co-glycolic acid</td>
</tr>
<tr>
<td>Sirolimus+EPC capture, OrbusNeich</td>
<td>Cobalt-chromium 60 µm</td>
<td>Sirolimus 5µg/mm</td>
<td>SynBiosys polymer</td>
</tr>
<tr>
<td>Supralimus and Supralimus core, Sahajanand Medical</td>
<td>Stainless steel 81 µm</td>
<td>Sirolimus 4.7µg/mm</td>
<td>Poly L-lactide, poly DL-lactide-co-glycolide and polyvinyl pyrrolidone</td>
</tr>
</tbody>
</table>
Randomized trial of three rapamycin-eluting stents with different coating strategies for the reduction of coronary restenosis

Julinda Mehilli, Robert A. Byrne, Anna Wieczorek, Raisuke Iijima, Stefanie Schulz, Olga Bruskina, Jürgen Pache, Rainer Wessely, Albert Schömig, and Adnan Kastrati* for the Intracoronary Stenting and Angiographic Restenosis Investigators – Test Efficacy of Rapamycin-eluting Stents with Different Polymer Coating Strategies (ISAR-TEST-3)
Secondary endpoints

Binary angiographic restenosis at 6-month angiographic follow-up

ISAR-TEST 3

BP RES, biodegradable-polymer rapamycin-eluting stent;
PF RES, polymer-free rapamycin-eluting stent;
PP RES, permanent-polymer rapamycin-eluting stent

### Stent thrombosis at 1 year

<table>
<thead>
<tr>
<th></th>
<th>Biodegradable polymer (n = 202)</th>
<th>Permanent polymer (n = 202)</th>
<th>Polymer-free (n = 201)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite</td>
<td>0 (0.0)</td>
<td>1 (0.5)</td>
<td>2 (1.0)</td>
</tr>
<tr>
<td>Probable</td>
<td>1 (0.5)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Possible</td>
<td>1 (0.5)</td>
<td>3 (1.5)</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>All</td>
<td>2 (1.0)</td>
<td>4 (2.0)</td>
<td>3 (1.5)</td>
</tr>
</tbody>
</table>

Randomized, non-inferiority trial of three limus agent-eluting stents with different polymer coatings: the Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents (ISAR-TEST-4) Trial

Table 5  Stent thrombosis at 1 year according to Academic Research Consortium criteria

<table>
<thead>
<tr>
<th></th>
<th>Biodegradable polymer DES, n = 1299</th>
<th>Permanent polymer DES, n = 1304</th>
<th>Relative risk (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite</td>
<td>8 (0.6)</td>
<td>12 (1.0)</td>
<td>0.67 (0.27–1.62)</td>
<td>0.37</td>
</tr>
<tr>
<td>Probable</td>
<td>5 (0.4)</td>
<td>7 (0.6)</td>
<td>0.71 (0.23–2.23)</td>
<td>0.56</td>
</tr>
<tr>
<td>Possible</td>
<td>6 (0.5)</td>
<td>7 (0.6)</td>
<td>0.85 (0.29–2.53)</td>
<td>0.77</td>
</tr>
<tr>
<td>Definite or probable</td>
<td>13 (1.0)</td>
<td>19 (1.5)</td>
<td>0.68 (0.34–1.38)</td>
<td>0.29</td>
</tr>
</tbody>
</table>
New concepts for drug release

“Discrete” system

“Homogeneous” system
Clinical trial

Patients with ischemic myocardial symptoms related to de novo lesions (max 2 in 2 different vessels) in native coronary arteries

CID DES
(n=150 pts)
Ø 3.0 – 3.5 mm
L 12 -16 – 20 – 25 mm

11 European Sites
Randomisation 1:1
100% angiographic f-up
20% IVUS f-up
PI: Prof Carrié - Fr

TAXUS LIBERTÉ
(n=150 pts)
Ø 3.0 – 3.5 mm
L 12 -16 – 20 – 25 mm

Primary Endpoint:

• LLL in-stent at 6 months post-procedure

Secondary Endpoints:

• QCA measurements in-stent and in-segment at 6 months
• IVUS measurements at 6 months (20%)
• Clinical composite occurrence of death, MI, any revascularization at 1 and 6 months, and yearly up to 5 years
• Thrombosis throughout the study duration, according to ARC definition
The design of the BioFreedom stent

Electron microscopy of BioFreedom stent platform with a textured abluminal surface
Biofreedom: In-Stent Angiographic Results

% Diameter Stenosis*

- BioFreedom SD: 7.6
- BioFreedom LD: 10.1
- Taxus Liberte: 18

Late Loss (mm)*

- BioFreedom SD: 0.08
- BioFreedom LD: 0.12
- Taxus Liberte: 0.37

*median values
Translumina Porous Surface Stent

Unique microporous stent surface

before coating after

Pure Sirolimus
Drug Filled Stent (DFS) Concept (Medtronic)

Drug elution controlled by diffusion physics

No Polymer!
# DES polymer free

<table>
<thead>
<tr>
<th>DES</th>
<th>Stent platform</th>
<th>Drug</th>
<th>Carrier system all abluminal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amazon Pax, MINVASYS</td>
<td>Cobalt- chromium 73µm</td>
<td>Paclitaxel 2.5µg/mm</td>
<td>Coating</td>
</tr>
<tr>
<td>BioFreedom, Biosensors</td>
<td>Stainless steel 119 µm</td>
<td>Biolimus A9</td>
<td>Surface modification with coating</td>
</tr>
<tr>
<td>Optima, CID</td>
<td>Stainless steel 137 µm</td>
<td>Tacrolimus 2.3µg/mm</td>
<td>Carbofilm and reservoirs</td>
</tr>
<tr>
<td>XX,CID</td>
<td>Cobalt-chromium 87 µm</td>
<td>Sirolimus 2.3µg/mm</td>
<td>Carbofilm, reservoirs with stearic acid</td>
</tr>
<tr>
<td>VESTAsync, MIV Therap.</td>
<td>Stainless steel 65 µm</td>
<td>Sirolimus 2.9µg/mm</td>
<td>Microporous hydroxyapatite</td>
</tr>
<tr>
<td>YUKON Choice, Translumina</td>
<td>Stainless steel 87 µm</td>
<td>Sirolimus 120µg/cm² and probucol 100µg/cm²</td>
<td>Microporous surface</td>
</tr>
</tbody>
</table>
### Metallic stents with novel coating “Non-Drug-Eluting Stents”

<table>
<thead>
<tr>
<th>Type of stent</th>
<th>Coating</th>
<th>Platform Thickness $\mu$m</th>
<th>Late loss, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chrono; AvantGarde CID</td>
<td>Carbon</td>
<td>Cobalt-Chromium 70</td>
<td>0.60 registry</td>
</tr>
<tr>
<td>Catania CeloNova</td>
<td>Polyzene</td>
<td>Cobal-Chromium 65-74</td>
<td>0.60 registry</td>
</tr>
<tr>
<td>TINOX Hexacath</td>
<td>Titanium Nitride-oxide</td>
<td>Stainless Steel 90</td>
<td>0.55 randomized</td>
</tr>
<tr>
<td>Genous</td>
<td>CD34 antibody</td>
<td>Stainless Steel 100</td>
<td>1.14 randomized</td>
</tr>
</tbody>
</table>
Conclusions

Improvements between 1° (Cypher and Taxus) and 2° Generation stents (Xience V, Promus) have been quite significant raising the standards to new levels that 3° Generation stents will have to confront:

Performance in Diabetics

Duration of Dual Antiplatelet Therapy