“EXCEL” Drug Eluting Stent in Real World Experience: Medium-to-long term follow-up

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Background

- Drug-eluting stents represent a major advance in the field of interventional cardiology & the marked reduction in restenosis rate has led to overwhelming enthusiasm in the medical world.

- Two major issues of its wide application are:
  - **Safety of polymer**: potential for increased inflammatory & thrombogenic responses & life threatening consequences
  - **Cost**

- “MEDISTRA” is a single center, open label, “first-in-man” (FIM) study of “EXCEL”, a “less costly” sirolimus-eluting stent using biodegradable polymer in real world cases.
"EXCEL":
A NEW SIROLIMUS-ELUTING STENT

Platform:
S-Stent

Drug:
Sirolimus

Carrier:
Biodegradable Poly-lactic acid polymer

EXCEL

Safe
Efficacious
Less costly
The Platform: “S-Stent”

- Highly flexible corrugated ring stent (laser-cut from a stainless tube)
- Each corrugated ring has 6 serially connected S-shaped segments
- 2 bend joints within each S-shaped segment

- Successive rings in the stent are connected by 2 short flexible links, with successive pairs of these links oriented in 90° quadrature around the circumference of successive rings (Quadrature links)
The Platform: “S-Stent”

- Highly flexible
- Reduced expansion forces required to deploy the stent
- High hoop strength
- High vessel wall support both in straight & curved vessels
- Moderate radio-opacity, sufficient for correct placement by angiography
Acute and Long-Term Clinical and Angiographic Outcome After S-Stent Implantation: S-Stent Multicenter Safety and Efficacy Trial

Charles Chan,1* Yean-Leng Lim,1 PhD, Teguh Santoso,2 MD, Damras Tresukosol,3 MD, Yean-Teng Lim,4 Shinjo Sonoda,5 MD, and Peter Fitzgerald,5 MD

The purpose of this study is to demonstrate safety and effectiveness of the S-Stent in de novo coronary lesions treated with conventional percutaneous coronary balloon angioplasty. Between January 2000 and June 2001, 120 patients were prospectively enrolled at four study centers. Patients were treated with coronary stenting in a total of 137 lesions. Procedural success was achieved in 100% of 137 attempted lesions. Clinical success was 99.8%. In-hospital mortality was 0.8%; myocardial infarction occurred in 0.8% and stent thrombosis in 0.8%. After stent implantation, the minimal lumen diameter increased from 0.92 ± 0.43 to 2.74 ± 0.36 mm (P < 0.0001) and the percent diameter stenosis decreased from 68.0 ± 16.2 to 4.5 ± 12.0 (P < 0.0001). At 6-month follow-up, the percent diameter stenosis was 33.5 ± 21.3 and the angiographic restenosis rate was 16.5%. Target lesion revascularization was required in 12 patients (10.1%). We conclude that the use of S-Stent for coronary intervention resulted in a high procedural success rate and low angiographic restenosis at 6 months after implantation. Catheter Cardiovasc Interv 2004;62:439–444.

Key words: Biosensors S-Stent; clinical outcome; restenosis
“EXCEL” : A Sirolimus-Eluting Stent

- Very thin coating on the stent
- Ideal coating-tissue interaction (asymmetrical polymer / drug coating: more drug is exposed to the vessel wall & less to the artery)
28-day Preclinical Study Results

without Sirolimus

with Sirolimus
Medistra Excel Drug-Eluting Stent TRIAL

- Single center, prospective, observational study (Medistra Hospital) (January 30, 2004 – February 28, 2006)

- Study NOT sponsored by the company

- Inclusions:
  - All comers who are candidates for PCI ("real world cases")

- Exclusions:
  - Contraindications to anti-platelets
  - Patients with short life expectancy & serious concomitant disease (advanced cancer, etc)
  - Lack of patient’s consent
**Medistra Excel Drug-Eluting Stent TRIAL**

- **Primary End-Point:**
  - TLR at 6 and 12 months

- **Secondary End-Point:**
  - 6-month in-segment restenosis rate
  - In-segment late loss
  - Major Adverse Cardiac Events (MACE):
    - Death, QMI, NQMI, & / or TLR

QCA analysis is done by an independent core laboratory
(National Heart Heart Heart Center - Singapore)
(Dr. A. Wong, Prof. Tian-Hai Koh)
Predilatation is encouraged, even though direct stenting is allowed in simple lesion.

Stent selection:
- Try to always use Excel
- If appropriate size / length not available, use other DES (Cypher or Taxus)
- If other DES is not available (logistic problem), use BMS

Antiplatelet regimen:
- ASA 160 mg indefinitely (unless contraindicated)
- Clopidogrel 300 mg (loading), then 75 mg for 6 months
Methods

All comers, 
N = 279

2 stent dislodgement* ("prototype stent")

277 eligible pts

DES-tenting as default strategy (N=771), except if there is logistic problem (BMS will be used)

EXCEL
N=470

CYPHER
N=137

TAXUS
N=86

BIOMATRIX
N=27

ENDEAVOUR
N=5

BMS
N=46

* 1 case when negotiating mildly stenotic, acutely angulated LCX to fix mid-LCX stenosis
1 case with diffuse, calcified mid_RCA stenosis, during attempted direct stenting
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>277</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>58.5 ± 9.4</td>
</tr>
<tr>
<td>Male / female</td>
<td>226/51</td>
</tr>
<tr>
<td>Family history</td>
<td>97 (35.0%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>152 (54.9%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>160 (57.8%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>110 (39.7%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>119 (43.0%)</td>
</tr>
<tr>
<td>Prior MI</td>
<td>123 (44.4%)</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>14 (5.0%)</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>77 (22.8%)</td>
</tr>
</tbody>
</table>
## Clinical Presentation

<table>
<thead>
<tr>
<th></th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>277</td>
</tr>
<tr>
<td>No lesions</td>
<td>631</td>
</tr>
<tr>
<td>No stents</td>
<td>771</td>
</tr>
</tbody>
</table>

### Clinical presentation

- **Stable angina**: 133 (48.0%)
- **Unstable angina / ACS**: 32 (11.6%)
- **Acute MI**: 11 (4.0%)
- **Recent MI ( < 30 days)**: 15 (5.4%)
- **Silent ischemia**: 86 (31.0%)

- **LVEF (%, mean ± SD)**: 59 ± 11%
Cumulative Patient Recruitment & Excel stent utilization

EXCEL stents

patients

12 months
Extent of Disease

N of pts

<table>
<thead>
<tr>
<th>Extent of Disease</th>
<th>N of pts</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVD</td>
<td>103</td>
<td>(37.2%)</td>
</tr>
<tr>
<td>DVD</td>
<td>107</td>
<td>(38.6%)</td>
</tr>
<tr>
<td>TVD</td>
<td>54</td>
<td>(19.5%)</td>
</tr>
<tr>
<td>LM-SVD</td>
<td>8</td>
<td>(2.9%)</td>
</tr>
<tr>
<td>LM-DVD</td>
<td>3</td>
<td>(1.0%)</td>
</tr>
<tr>
<td>LM-TVD</td>
<td>1</td>
<td>(0.4%)</td>
</tr>
<tr>
<td>LM only</td>
<td>1</td>
<td>(0.4%)</td>
</tr>
</tbody>
</table>
De-Novo Suboptimal Bail-out

Indications for Stenting

- EXCEL
- TAXUS
- CYPHER
- BIOMATRIX
- ENDEAVOUR
- BMS

N

Bar chart showing the number of indications for stenting in De-Novo, Suboptimal, and Bail-out categories.
Types of Lesion
Stent length

N of stent

- EXCEL
- TAXUS
- CYPHER
- BIOMATRIX
- ENDEAVOUR
- BMS

N of stent length
- <15
- 15-19
- 20-24
- >=25

mm
Stent size

**EXCEL (N = 470)**
- 2.5 mm: 37%
- 3.0 mm: 15%
- 3.5 mm: 15%

**TAXUS (N = 86)**
- 2.5 mm: 30%
- 3.0 mm: 33%
- 3.5 mm: 22%

**CYPHER (N = 137)**
- 2.5 mm: 31%
- 3.0 mm: 9%
- 3.5 mm: 27%

**BMS (N = 46)**
- 2.5 mm: 22%
- 3.0 mm: 22%
- 3.5 mm: 17%

**BIOMATRIX (N = 27)**: 2.5 mm: 16; 3 mm: 5; 3.5 mm: 3; 4 mm: 3

**ENDEAVOUR (N = 5)**: 2.5 mm: 2; 3 mm: 2; 3.5 mm: 2
### Results

#### In-hospital outcome

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (pts)</td>
<td>277</td>
<td>100%</td>
</tr>
<tr>
<td>Cardiac deaths</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Noncardiac deaths</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Nonfatal QMI</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Nonfatal NQMI</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Any nonfatal MI</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Acute thrombosis</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
Results

30-day clinical outcome

- No (pts) 232 (83.8%)
- Cardiac deaths 2**
- Noncardiac deaths 0
- Nonfatal QMI 0
- Nonfatal NQMI 0
- Any nonfatal MI 0
- CABG 0
- TVR 1*
- Subac. thrombosis 2*

* Pt has very diffuse ultra-small LAD disease & multiple overlapped Cypher & Excel stents
+Pt had triple, small vessel disease & died 1 week after PCI & had 5 stents (Excel, Biomatrix & Cypher stents)
Results

6-month clinical outcome

- No (pts) 210 (75.8%)
- Cardiac deaths 2
- Noncardiac deaths 0
- Nonfatal QMI 0
- Nonfatal NQMI 0
- Any nonfatal MI 0
- CABG 0
- TVR 4
- Late thrombosis 0
## Results

### 12-month clinical outcome

<table>
<thead>
<tr>
<th>Event</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (pts)</td>
<td>154 (50.5%)</td>
</tr>
<tr>
<td>Cardiac deaths</td>
<td>2</td>
</tr>
<tr>
<td>Noncardiac deaths</td>
<td>0</td>
</tr>
<tr>
<td>Nonfatal QMI</td>
<td>0</td>
</tr>
<tr>
<td>Nonfatal NQMI</td>
<td>0</td>
</tr>
<tr>
<td>Any nonfatal MI</td>
<td>0</td>
</tr>
<tr>
<td>CABG</td>
<td>0</td>
</tr>
<tr>
<td>TVR</td>
<td>6</td>
</tr>
<tr>
<td>Late thrombosis</td>
<td>0</td>
</tr>
</tbody>
</table>
QCA analysis at 6 months

QCA analysis: 94 pts with 217 lesions.
Vessels & number of lesions treated:
- LAD/D = 97, LCX/OM = 63, RCA = 51; LM = 6

Types of Stents used (per lesion)

<table>
<thead>
<tr>
<th></th>
<th>Cypher (n=34)</th>
<th>Taxus (n=30)</th>
<th>Excel (n=138)</th>
<th>BMS (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>15.8</td>
<td>18.3</td>
<td>15.8</td>
<td>12.3</td>
</tr>
<tr>
<td>Stent size (mm)</td>
<td>2.85</td>
<td>2.87</td>
<td>2.86</td>
<td>3.50</td>
</tr>
<tr>
<td>Stent length (mm)</td>
<td>22.5</td>
<td>26.8</td>
<td>21.7</td>
<td>16.8</td>
</tr>
</tbody>
</table>
## QCA analysis at 6 months

<table>
<thead>
<tr>
<th></th>
<th>CYPHER</th>
<th>TAXUS</th>
<th>EXCEL</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre procedural</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVD, mm</td>
<td>2.60</td>
<td>2.57</td>
<td>2.53</td>
<td>3.20</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>0.93</td>
<td>0.95</td>
<td>0.97</td>
<td>1.09</td>
</tr>
<tr>
<td>DS, %</td>
<td>57.3</td>
<td>62.2</td>
<td>60.0</td>
<td>66.0</td>
</tr>
<tr>
<td><strong>Post procedural</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVD, mm</td>
<td>2.61</td>
<td>2.61</td>
<td>2.53</td>
<td>3.17</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>2.13</td>
<td>2.11</td>
<td>2.08</td>
<td>2.73</td>
</tr>
<tr>
<td>DS, %</td>
<td>17.7</td>
<td>18.8</td>
<td>17.7</td>
<td>12.8</td>
</tr>
<tr>
<td>Stent MLD, mm</td>
<td>2.28</td>
<td>2.29</td>
<td>2.33</td>
<td>2.76</td>
</tr>
<tr>
<td>In-stent DS, %</td>
<td>12.1</td>
<td>11.5</td>
<td>7.23</td>
<td>12.2</td>
</tr>
<tr>
<td><strong>Follow-up (6 months)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RVD, mm</td>
<td>2.67</td>
<td>2.60</td>
<td>2.64</td>
<td>3.22</td>
</tr>
<tr>
<td>MLD, mm</td>
<td>1.89</td>
<td>1.78</td>
<td>2.07</td>
<td>2.06</td>
</tr>
<tr>
<td>DS, %</td>
<td>29.2</td>
<td>31.7</td>
<td>21.6</td>
<td>35.9</td>
</tr>
<tr>
<td>Stent MLD, mm</td>
<td>2.03</td>
<td>1.92</td>
<td>2.26</td>
<td>2.06</td>
</tr>
<tr>
<td>In-stent DS, %</td>
<td>24.0</td>
<td>26.3</td>
<td>14.2</td>
<td>35.9</td>
</tr>
</tbody>
</table>
# Follow-up (6 months)

### Late loss, mm

<table>
<thead>
<tr>
<th>Group</th>
<th>CYPHER</th>
<th>TAXUS</th>
<th>EXCEL</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-segment</td>
<td>0.24</td>
<td>0.31</td>
<td>0.01</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>(p=0.12)</td>
<td>(p=0.03)</td>
<td>(p=0.003)</td>
<td></td>
</tr>
<tr>
<td>In-stent</td>
<td>0.25</td>
<td>0.35</td>
<td>0.07</td>
<td>0.59</td>
</tr>
<tr>
<td></td>
<td>(p=0.055)</td>
<td>(p=0.004)</td>
<td>(p&lt;0.001)</td>
<td></td>
</tr>
</tbody>
</table>

### Restenosis (>50%), n

<table>
<thead>
<tr>
<th>Group</th>
<th>CYPHER</th>
<th>TAXUS</th>
<th>EXCEL</th>
<th>BMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-segment</td>
<td>6/33 (18.2%)</td>
<td>3/30 (10%)</td>
<td>7/135 (5.2%)</td>
<td>2/12 (16.7%)</td>
</tr>
<tr>
<td></td>
<td>(p=0.012)</td>
<td>(p=NS)</td>
<td>(p=NS)</td>
<td></td>
</tr>
<tr>
<td>In-stent</td>
<td>5/33 (15.2%)</td>
<td>2/30 (10%)</td>
<td>5/135 (3.7%)</td>
<td>2/12 (16.7%)</td>
</tr>
<tr>
<td></td>
<td>(p=0.013)</td>
<td>(p=NS)</td>
<td>(p=NS)</td>
<td></td>
</tr>
</tbody>
</table>
Cumulative Distribution Curves for EXCEL Stent

Excel

Minimal Luminal Diameter (mm)

Cumulative Percent

Pre
Post
F/U
Cumulative Distribution Curves for All Stents

- **EXCEL**
- **CYPHER**
- **TAXUS**
- **Bare metal stent**
**Instent Restenosis of RCA**

Baseline:
Focal instent restenosis of a Bard stent

Post- stenting:
Excel 3.0/18

6 month f/up:
No restenosis
Acute Myocardial Infarction

Baseline

After thrombus aspiration w/ percu-surge

TedAD, M, 45, AMI

After stenting

Excel 3/24

6 mo f/up
Very long / diffuse LAD stenosis

GeGnwn, M, 62, silent ischemia

Baseline:
Diffuse LAD stenosis

After placement of 2 overlapping Excel stents
(2.5/28 & 3.0/28 mm)

No restenosis at 6 months angiogr. f/up
LM ostial stenosis:
Restenosis of TAXUS stent treated w/ EXCEL stent

Baseline: LM ostial stenosis

Post stenting (TAXUS 3.5/12)

Restenosis at 6 months

Post stenting (EXCEL 3.5/14)

6 month after EXCEL implantation
Baseline: CTO in LAD

After placement of 2 overlapping Excel stents (2.5/18 & 3.0/18 mm)

No restenosis at 6 months angiogr. f/up

IskS, M, 63, Stable angina

**Triple CTO (LAD/LCX/RCA)**
Triple CTO (LAD/LCX/RCA)

IskS, M, 63, Stable angina

Baseline: CTO in RCA

After placement of 3 overlapping Excel stents (3/14; 3/18; 3/14 mm)

RCA

No restenosis at 6 months angiogr. f/up
Triple CTO (LAD/LCX/RCA)

IskS, M, 63, Stable angina

Baseline: CTO in LCX

After placement of Excel stent (2.5/18 mm)

No restenosis at 6 months angiogr. f/up
6 month f/up:
Prox. persistent restenosis

SariP, 50, SAP

Excel
3.0/14

Post-stenting:
Excel stent too short

Baseline

6 month f/up:
Prox. persistent restenosis

Persistent restenosis (incomplete lesion coverage)
Bifurcation stenosis in LCX with instent restenosis (cypher)
**Diffuse, small vessel disease with CTO in LAD (1)**

Baseline: Diffuse, small vessel disease (dotted line) with CTO (arrow).

After placement of very long overlapping Excel (2.5/28 mm) & Cypher (2.5/23; 3/33; 3/13 mm) stents.
Diffuse, small vessel disease with CTO in LAD (2)

After placement of very long overlapping Excel (2.5/28 mm) & cypher (2.5/23; 3/33; 3/13 mm) stents

Occlusion of Cypher (& Excel) stent. TLR not performed as distal LAD was filled by collaterals from RCA
Conclusion

Despite the inclusion of challenging “real world cases” (DM, MVD, small vessel, complex lesions, long – diffuse disease, calcified stenosis, ostial stenosis, LM, AMI, CTO, instent restenosis, etc) the preliminary results are encouraging, with very low MACE rate & “clean” angiographic appearance of the stent on angiography