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

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Drug-eluting stents represent a major advance in the in the field of 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



### 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<sup>o</sup> 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

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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 angio-plasty. 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  $\pm$  0.43 to 2.74  $\pm$  0.36 mm (*P* < 0.0001) and the percent diameter stenosis decreased from 68.0  $\pm$  16.2 to 4.5  $\pm$  12.0 (*P* < 0.0001). At 6-month follow-up, the percent diameter stenosis was 33.5  $\pm$  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.  $\odot$  2004 Wiley-Liss, Inc.

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





# <u>Medistra Excel</u> <u>D</u>rug-Elut<u>Ing</u> <u>Stent</u> <u>TR</u>i<u>A</u>l

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

Study <u>NOT</u> 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

# <u>Medistra Excel</u> <u>D</u>rug-Elut<u>Ing</u> <u>Stent</u> <u>TRiAl</u>

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 Center - Singapore) (Dr. A. Wong, Prof. Tian-Hai Koh)

# <u>Medistra Excel</u> <u>Drug-Elut</u>Ing <u>Stent</u> <u>TRiAl</u>

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



\* 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

# Demography

#### 🗰 <mark>N</mark>

Age (yrs) Male / female Family history Hypertension Dyslipidemia Diabetes mellitus Smoking Prior MI Prior CABG Prior PCI

277 <u>58.5 +</u> 9.4 226/51 97 (35.0%) 152 (54.9%) 160 (57.8%) 110 (39.7%) 119 (43.0%) 123 (44.4%) 14 (5.0%) 77 (22.8%)

# **Clinical Presentation**

🛎 No	277
No lesions	631
No stents	771
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 <u>+</u> SD)	59 <u>+</u> 11%

### Cumulative Patient Recruitment & Excel stent utilization



# Extent of Disease



# **Vessel** location



# Indications for Stenting



# Types of Lesion



# Stent length



# Stent size



# Excel in Real World Cases



# Results In-hospital outcome

No (pts)	277 (100%
Cardiac deaths	0
Noncardiac deaths	0
Nonfatal QMI	0
Nonfatal NQMI	0
Any nonfatal MI	0
CABG	0
Acute thrombosis	0

## *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
	0
I 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
	0
TVR	4
Late thrombosis	0

# *Results* 12-month clinical outcome

No (pts)	154 (50.5%)
Cardiac deaths	2
Noncardiac deaths	0
Nonfatal QMI	0
Nonfatal NQMI	0
Any nonfatal MI	0
	0
TVR	6
Late thrombosis	0

### 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)

	Cypher	Taxus	Excel	BMS
	(n=34)	(n=30)	(n=138)	(n=15)
Lesion length(mm)	15.8	18.3	15.8	12.3
Stent size (mm)	2.85	2.87	2.86	3.50
Stent length (mm)	22.5	26.8	21.7	16.8

# QCA analysis at 6 months

	CYPHER	TAXUS	EXCEL	<u>BMS</u>	
Pre procedural					
RVD. mm	2.60	2.57	2.53	3.20	
MLD. mm	0.93	0.95	0.97	1.09	
DS, %	57.3	62.2	60.0	66.0	
Post procedural	1				
PUSt procedural	2 61	2 61	2 53	3 17	
MD mm	2.01	2.01	2.00	J.17 2 72	
	2.13	2.11 40.0	2.00	2.13	
DS, %	17.7	10.0	1/./	12.8	
Stent MLD, mm	2.28	2.29	2.33	2.76	
In-stent DS, %	12.1	11.5	7.23	12.2	
Follow-up (6 months)					
RVD. mm	2.67	2.60	2.64	3.22	
MLD, mm	1.89	1.78	2.07	2.06	
DS, %	29.2	31.7	21.6	35.9	
Stent MLD, mm	2.03	1.92	2.26	2.06	
In-stent DS, %	24.0	26.3	14.2	35.9	

QCA analysis at 6 months				
	<u>CYPHER</u>	TAXUS	EXCEL	<u>BMS</u>
Follow-up (6 mo	onths)(cont'd)			
Late loss, mm In-segment	0.24 ( <b>p=0.12)</b>	0.31 <b>(p=0.03)</b>	0.01	0.55 <b>(p=0.003)</b>
In-stent	0.25 <b>(p=0.055)</b>	0.35 <b>(p=0.004)</b>	0.07	0.59 <b>(p&lt;0.001)</b>
Restenosis (>50 <sup>°</sup> In-segment	<mark>%), n</mark> 6/33 (18.2%) <b>(p=0.012)</b>	3/30 (10%) <b>(p=NS)</b>	7/135 (5.2%)	2/12 (16.7%) <b>(p=NS)</b>
In-stent	5/33 (15.2%) <b>(p=0.013)</b>	2/30 (10%) <b>(p=NS)</b>	5/135 (3.7%)	2/12 (16.7%) <b>(p=NS)</b>

# Cumulative Distribution Curves for EXCEL Stent



### **Cumulative Distribution Curves for All Stents**





SariPD, 50, SAP













**Baseline**:

**Diffuse LAD stenosis** 

Very long / diffuse LAD stenosis

GeGnwn, M, 62, silent ischemia

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







IskS, M, 63, Stable angina



Baseline: CTO in LAD

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



IskS, M, 63, Stable angina



Baseline: CTO in RCA

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





IskS, M, 63, Stable angina



After placement of Excel stent (2.5/18 mm)



Post-stenting: Excel stent too short

Baseline

Peristent restenosis (incomplete lesion coverage)

Excel 3.0/14

6 month f/up: Prox. peristent restenosis



with instent restenosis (cypher)

Instent restenosis of the cypher at the bifurcation (& prox. end of Excel)

### Diffuse, small vessel disease with CTO in LAD (1)

HW, M, 45, OMI



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)

HW, M, 45, OMI



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 chalenging "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