

# **New Drug-Eluting Stents 2009**

***Martin B. Leon, MD***  
***(for Alexandre Abizaid, MD)***

***Columbia University Medical Center***  
***Cardiovascular Research Foundation***  
***New York City***

**Angioplasty Summit 2009 – TCT Asia Pacific**  
**April 22-24, 2009; Seoul, Korea**

**Presenter Disclosure Information for  
Angioplasty Summit 2009**

***Martin B. Leon, M.D.***

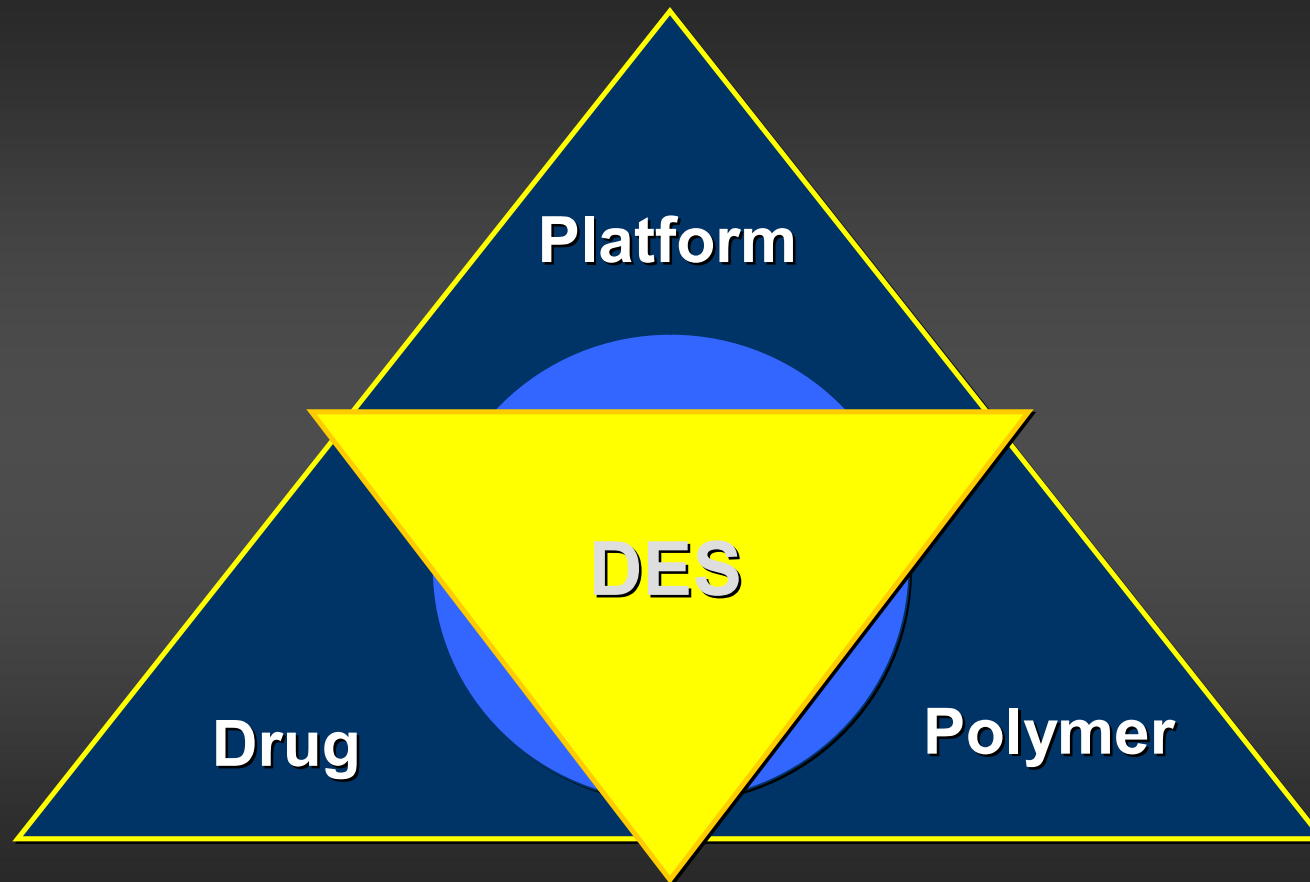
***Scientific Advisory Board or Equity:***  
Abbott, Boston Scientific, Cordis,  
and Medtronic



# Instituto Dante Pazzanese de Cardiologia: The Place of the First Drug Eluting Stent

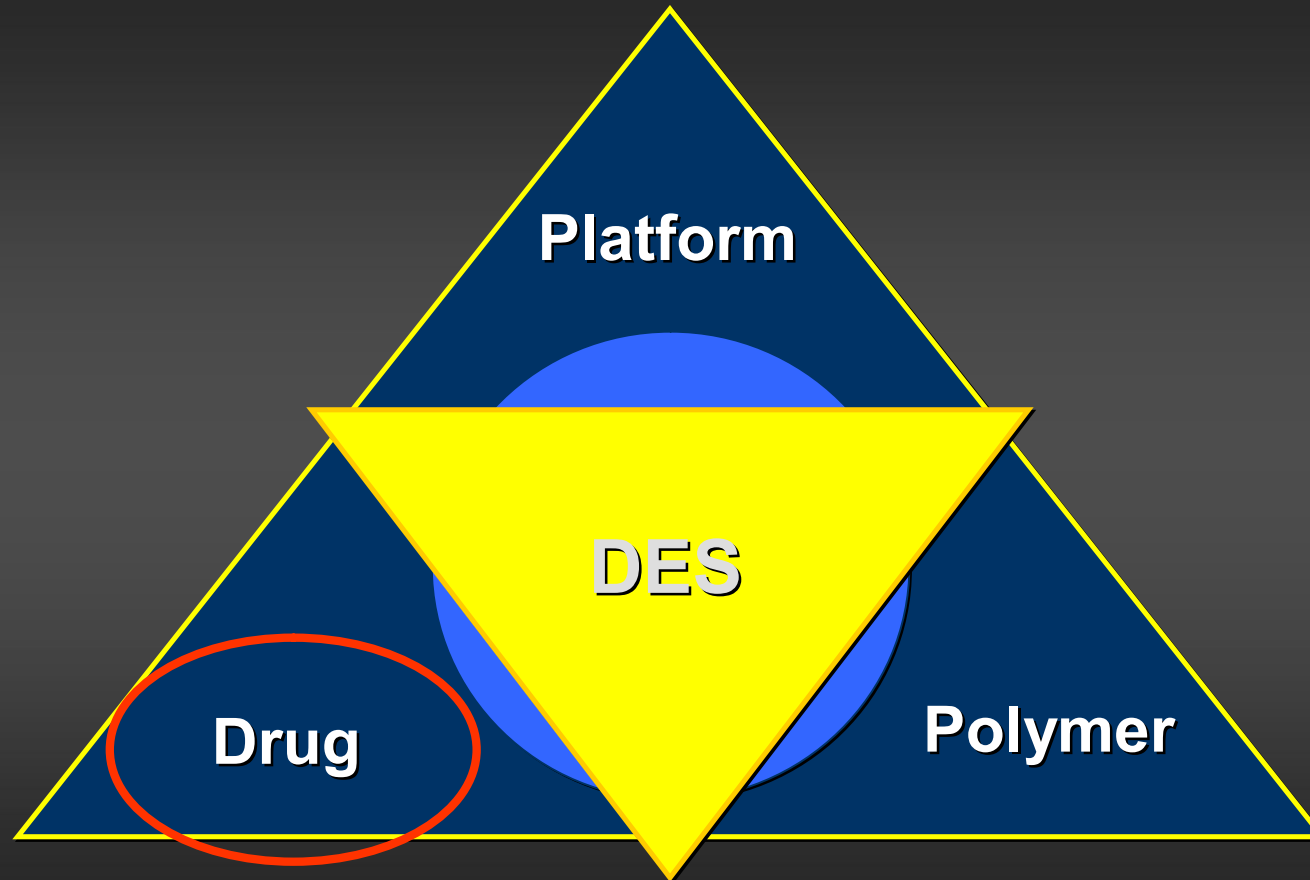


# The 3 Components of DES

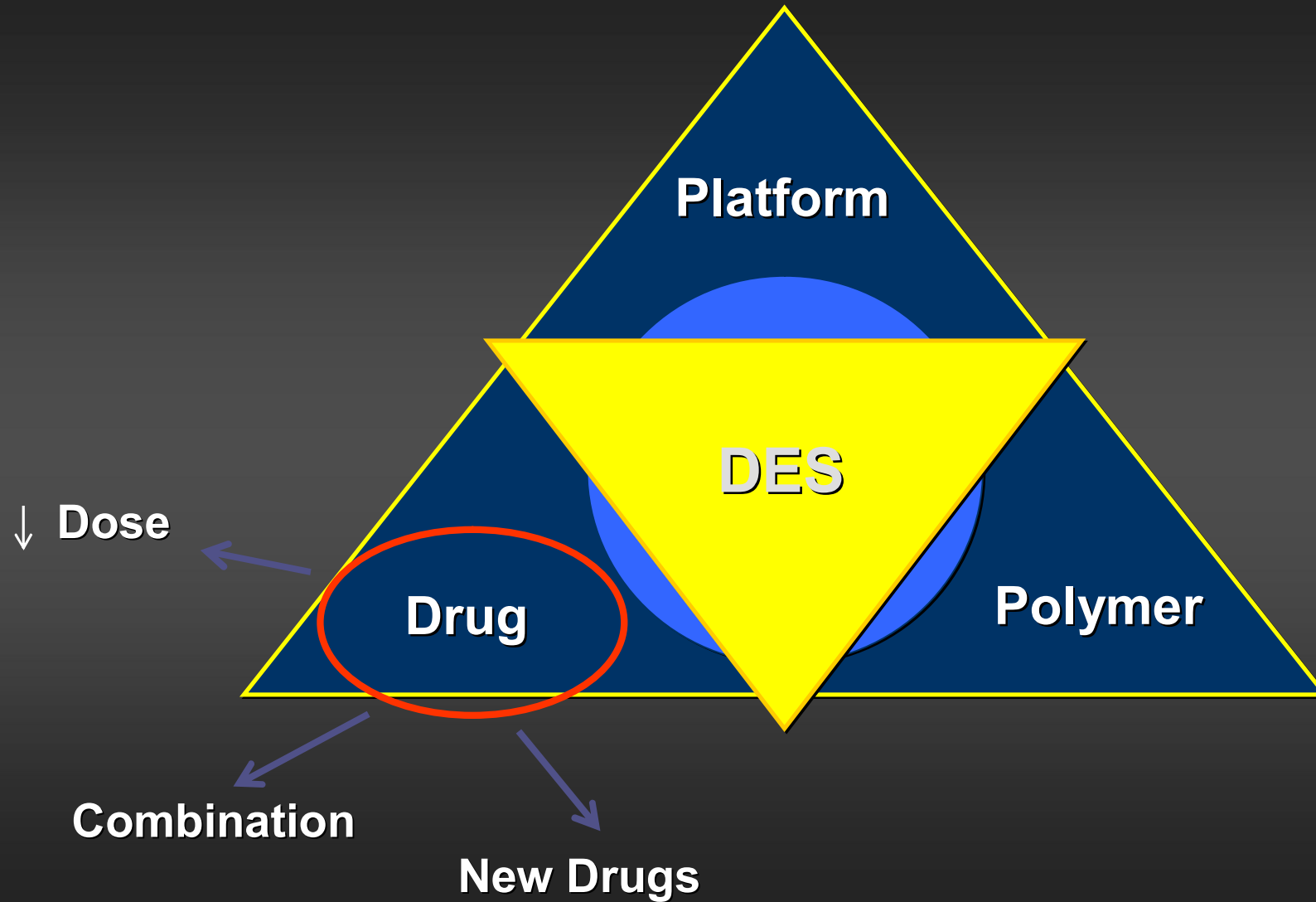




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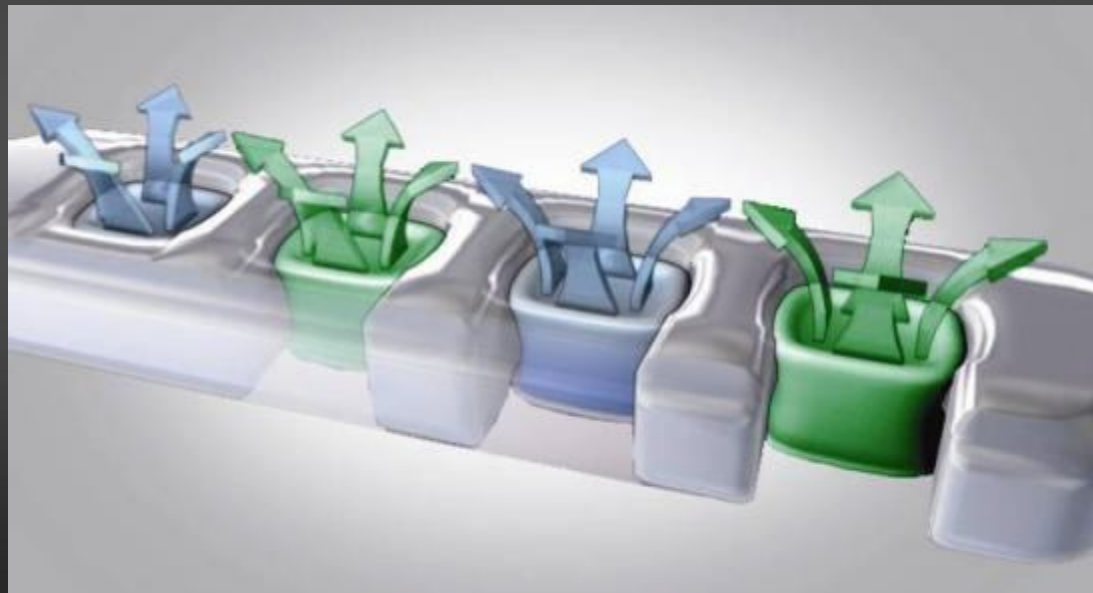


# The 3 Components of DES

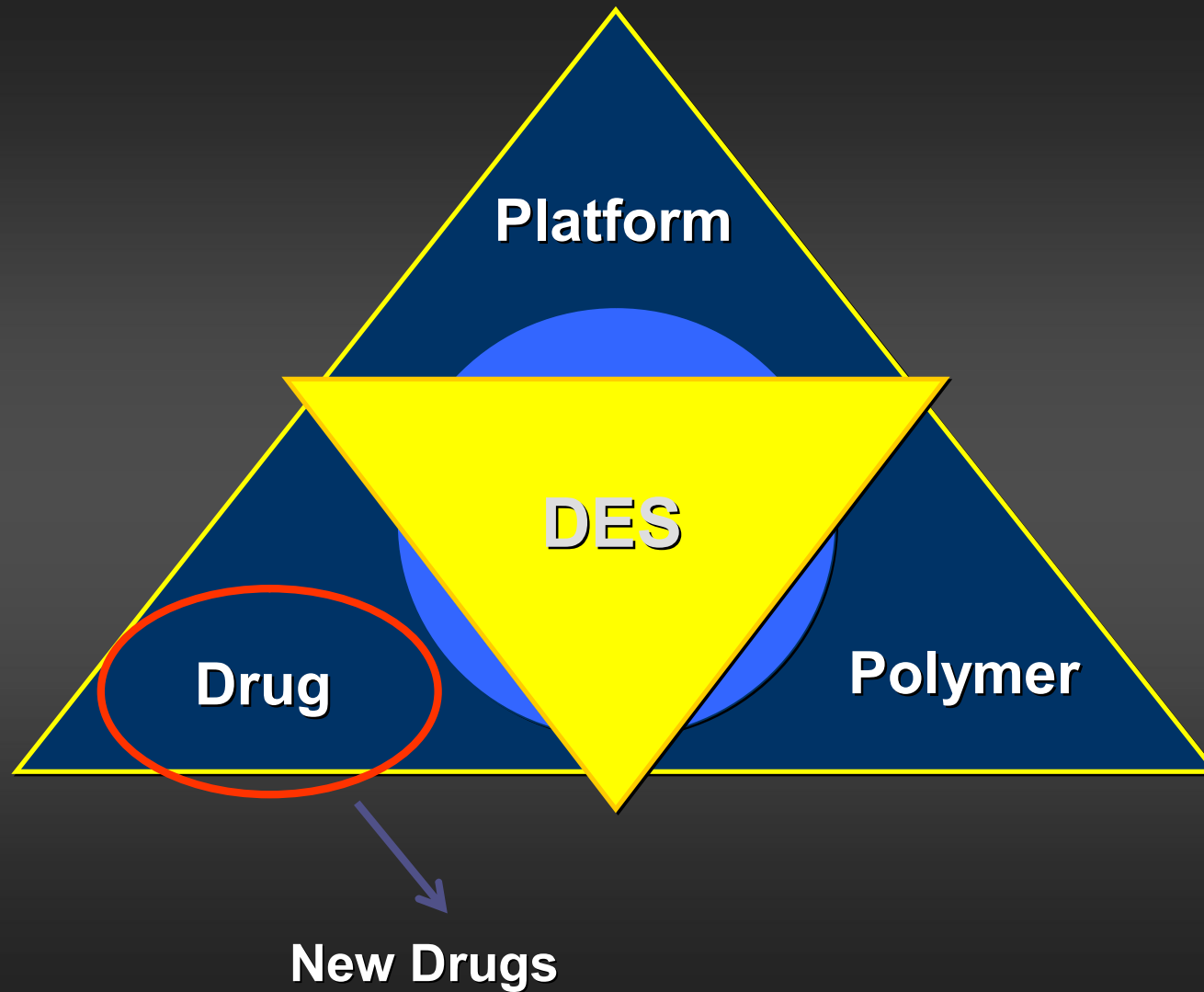


# Conor / Cordis Combination Stent System

Independent, Controlled Drug Release from Adjacent Reservoirs



# The 3 Components of DES



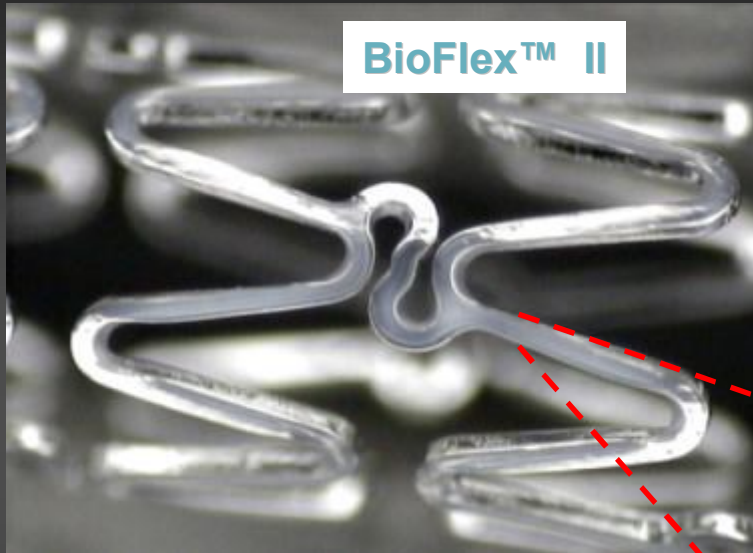


# New Drugs

- **Bioluminus (BioMatrix™ - Biosensors)**
- **Novoluminus (Exella™ - Elixir)**
- **Myoluminus (Epitome™ - Elixir)**

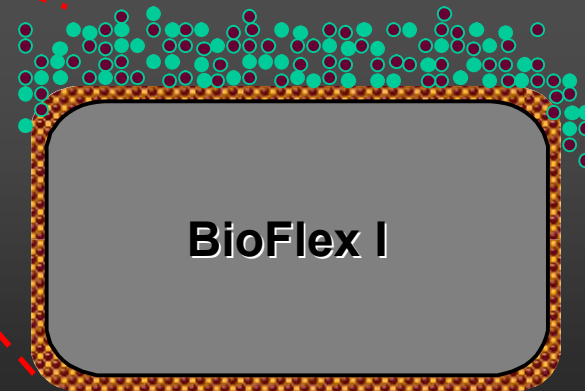
# BioMatrix<sup>®</sup> III Stent Platform

BIOMATRIX<sup>®</sup>



## Biodegradable Drug/Carrier:

- Biolimus A9<sup>®</sup> / Poly (Lactic Acid) 50:50 mix
- abluminal surface only (contacts vessel wall)
- 10 microns coating thickness
- degrades in 9 months releasing CO<sub>2</sub>+ water



# STEALTH (Abizaid, Grube)

STent Eluting A9 BioLimus Trial in Humans

First In-Man  
2:1 randomized  
n = 120

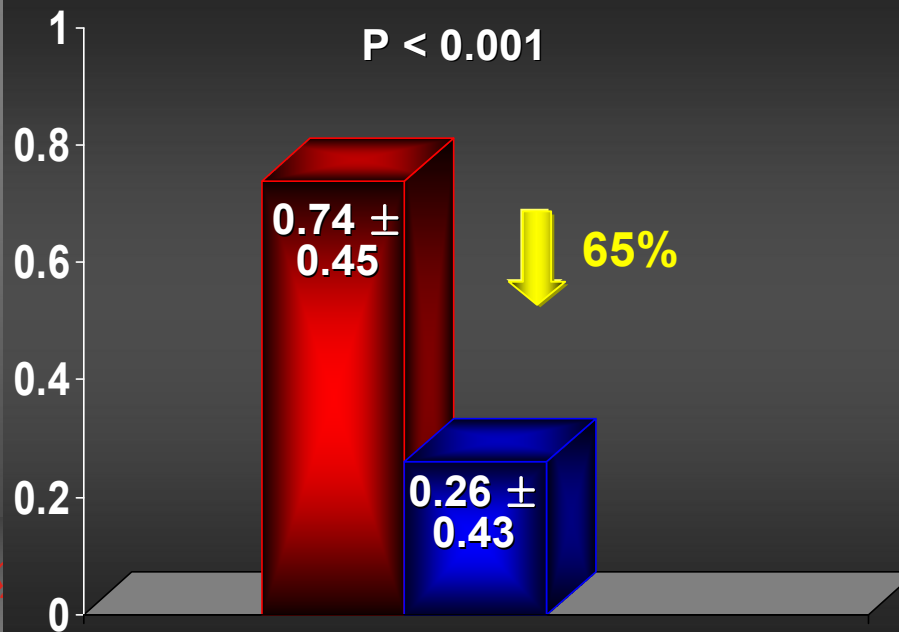
Biolimus A9 Eluting Stent  
n = 80

Control Bare Metal Stent  
n = 40

Primary Endpoint:  
Late Loss at 6  
Months

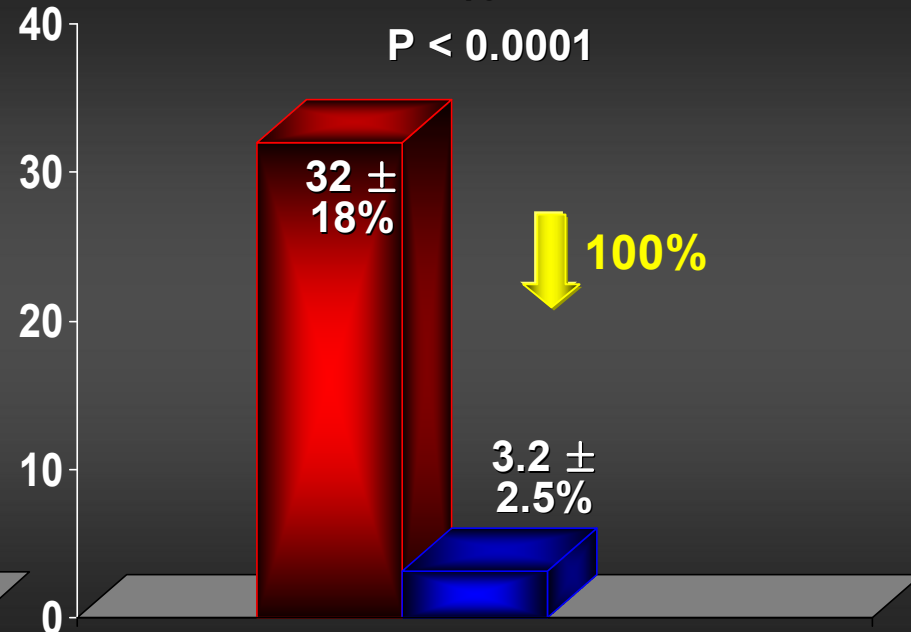
6-m In Stent Late Loss

P < 0.001



6-m IVUS % obstruction

P < 0.0001



# LEADERS: Trial Design

## Stable and ACS Patients Undergoing PCI

Assessor-blind  
1:1 Randomisation

N=1700 Patients

**Biolimus Stent**  
BioMatrix Flex N=850

**Sirolimus Stent**  
Cypher Select N=850

1:3 Randomisation

**Clinical F/U**  
N=640

**Angio F/U**  
N=210

**Clinical F/U**  
N=640

**Angio F/U**  
N=210

1° endpoint:

2° endpoints:

Angiographic study:

CV death, MI, clinically-indicated TVR

Death, CV death, MI, TLR, TVR

Stent Thrombosis according to ARC

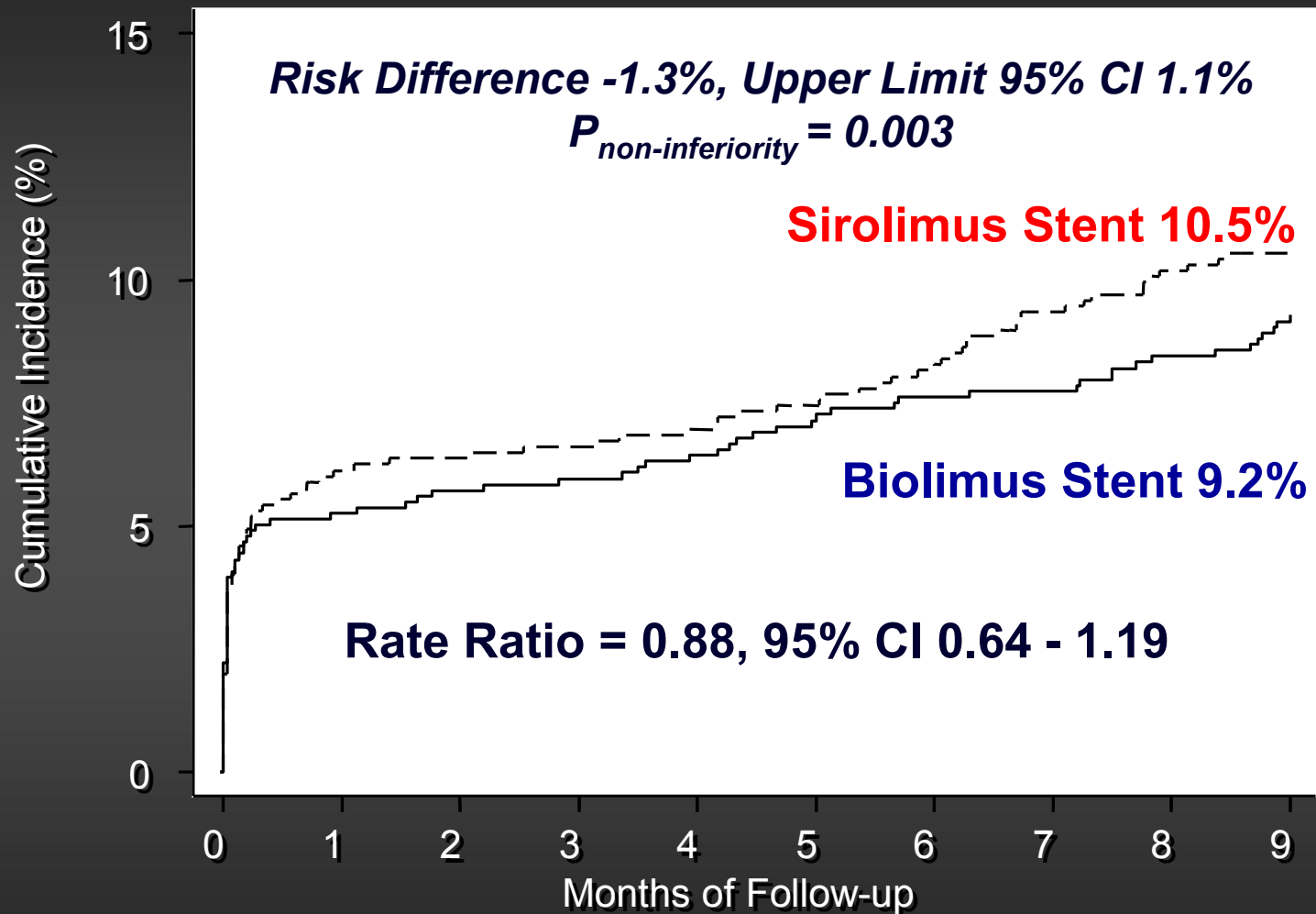
In-stent % diameter stenosis

Late loss, binary restenosis



# LEADERS: Primary Endpoint

Cardiac Death, MI, or TVR @ 9 months



No. at risk

BES	857	806	798	796	792	784	779	777	771	761
SES	850	791	786	784	781	777	771	758	751	746

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- **Novoluminus (Exella - Elixir)**
- **Myoluminus (Elixir)**

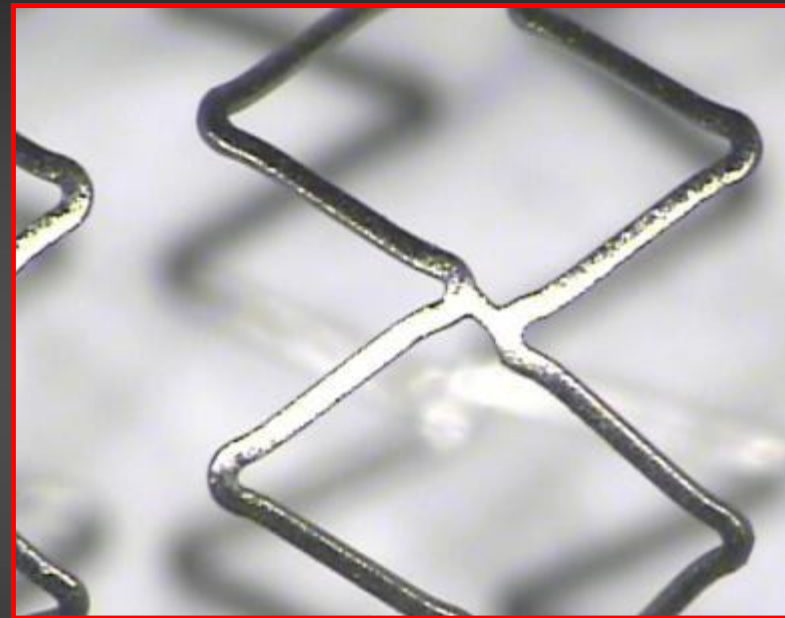
# The Elixir Novolimus-Eluting Stent

## Stent Design

- Cobalt-Chromium alloy
- 8 crown design for optimal scaffolding
- 0.0032" strut thickness

## Controlled Release Technology

- Methacrylate polymer family
  - Durable
- Biocompatible
- History of clinical use on vascular implants dose
- **Reduce dose (85  $\mu$ g) and polymer load (<3 microns)**



# Results

## Quantitative Coronary Angiography

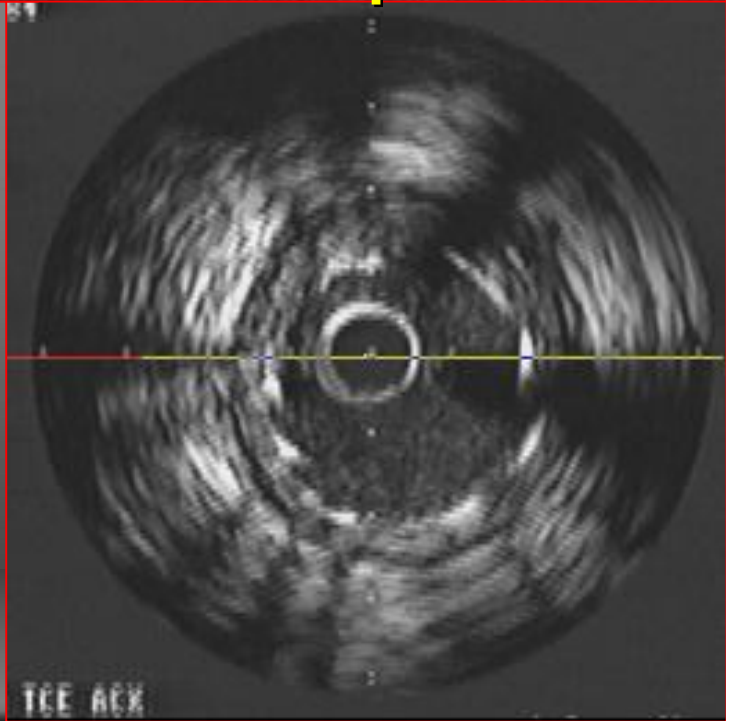
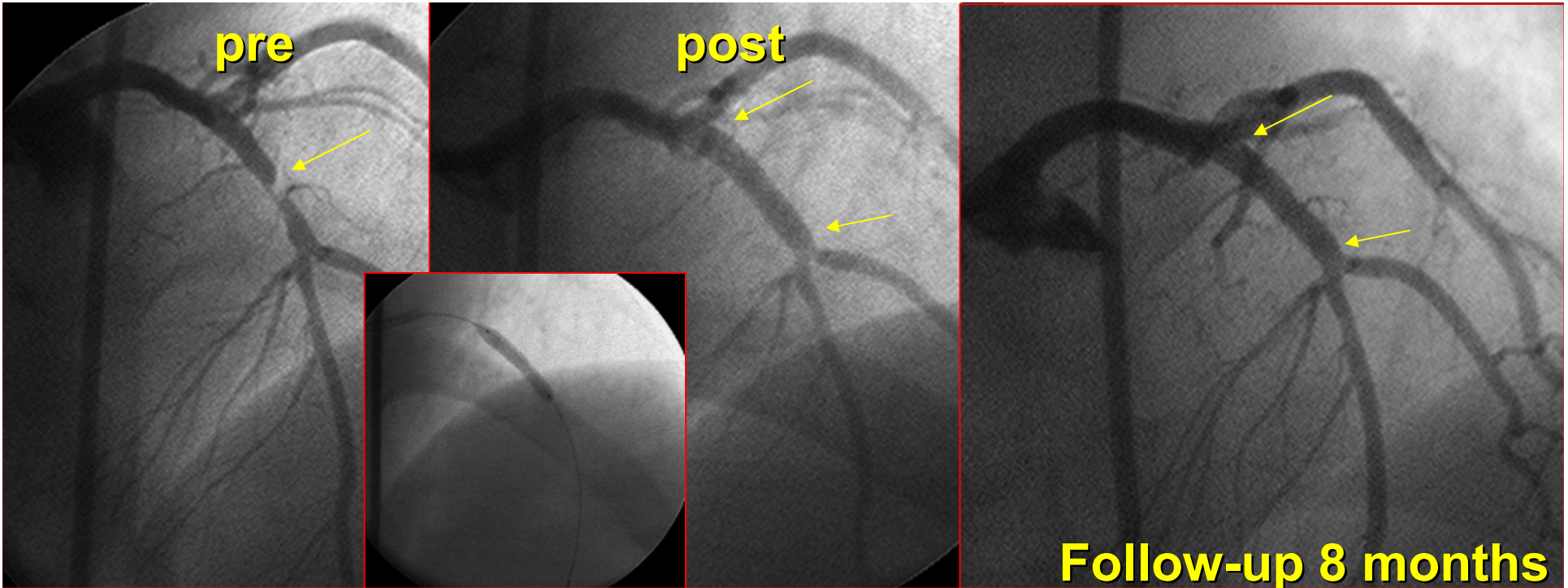
Variables	Lesions (n = 15)
<b>Pre-procedure</b>	
<i>Reference vessel diameter, mm</i>	2.7 ± 0.4
<i>Lesion length, mm</i>	8.7 ± 3.7
<i>Minimum lumen diameter, mm</i>	1.0 ± 0.3
<i>Diameter stenosis, (%)</i>	62.5 ± 8.6
<b>4-month follow-up</b>	
<i>Diameter stenosis, (%)</i>	12.5 ± 13.1
<i>Binary restenosis, (%)</i>	0
<i>Late loss</i>	0.15 ± 0.29
<b>8-month follow-up</b>	
<i>Minimum lumen diameter, mm</i>	2.7 ± 0.4
<i>Diameter stenosis, (%)</i>	18.2 ± 11.8
<i>Lumen loss, mm</i>	0.31 ± 0.25
<i>Binary restenosis, n(%)</i>	0



# IVUS Volumetric Analysis

## Baseline / 4 and 8-month follow-up

IVUS variables	Baseline N= 15 P	4-month follow-up N= 15 P	8-month Follow-up N=15p
Vessel Volume (mm <sup>3</sup> )	251.2 ± 78.8	259.7 ± 86.1	264 + 91.2
Stent Volume (mm <sup>3</sup> )	130.1 ± 39.7	134.0 ± 39.5	134.5 + 39.4
Lumen Volume (mm <sup>3</sup> )	129.9 ± 39.7	130.8 ± 40.0	127 + 41.8
NIH Volume (mm <sup>3</sup> )	N/A	3.2 ± 2.8	7.5 ± 3.9
% Stent Obstruction	N/A	2.7 ± 2.7	6.0 ± 4.4

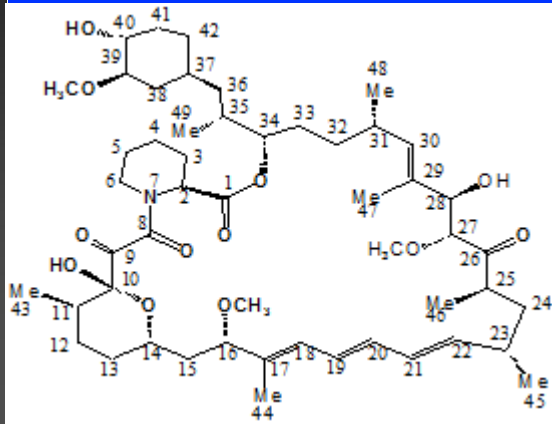


# New Drugs

- **Bioluminus (BioMatrix - Biosensors)**
- **Novoluminus (Exella - Elixir)**
- **Myoluminus ( Epitome - Elixir)**

# Elixir Myolimus DES with Bioabsorbable Polymer

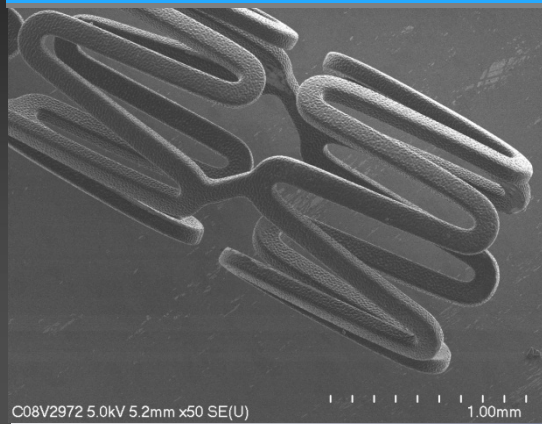
## Myolimus



Limus Family  
3 $\mu$ g per mm Stent  
Length

↓ Drug dose  
↑ Spatial distribution  
↑ Residual tissue conc.

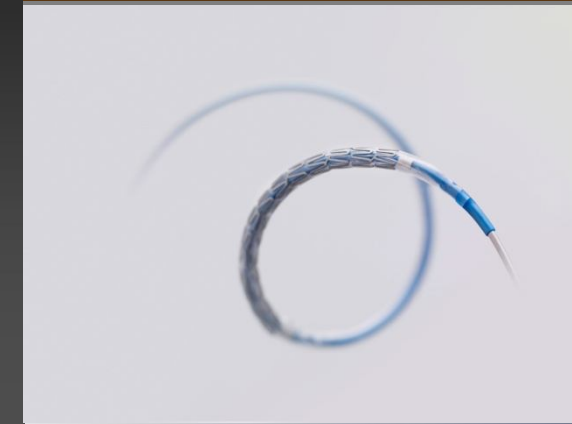
## Polymer



Cobalt Alloy Stent  
Bioabsorbable  
Polyester-based  
Polymer

↓ Strut thickness  
↑ Vessel coverage  
↓ Polymer load

## Platform



Nylon Blend Balloon

↑ Deliverability



# Elixir FIM Clinical Program

Pharmaceuticals

Novolimus  
Elixir

Myolimus  
Novartis

Polymers

Durable

Bioabsorbable

Durable

Bioabsorbable  
3-6m

Bioabsorbable  
6-9m

FIMs

FIM I  
ELX-0602

FIM II  
ELX-0802

FIM I  
ELX-0701

FIM II  
ELX-0703

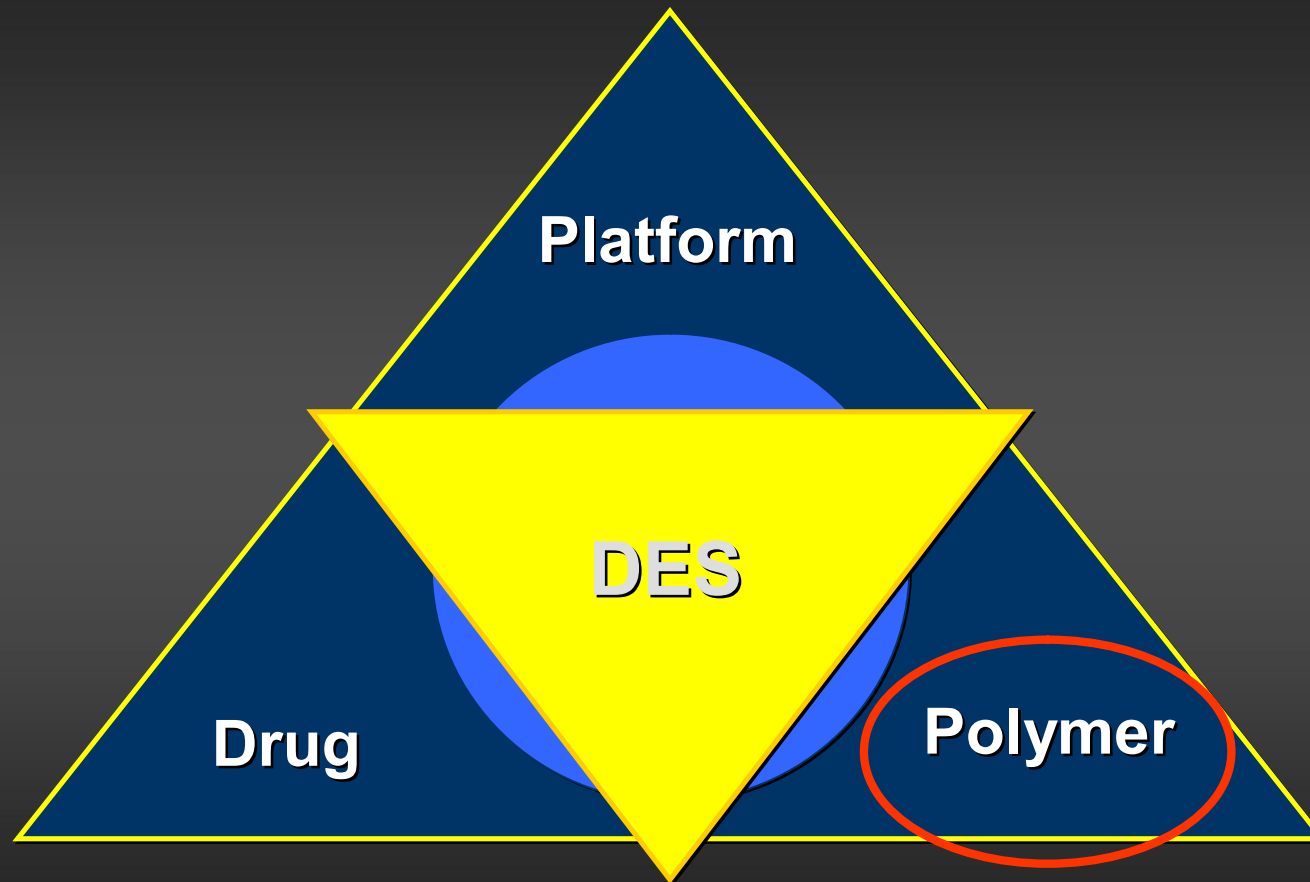
FIM III  
ELX-0704

CE Studies

EXCELLA II

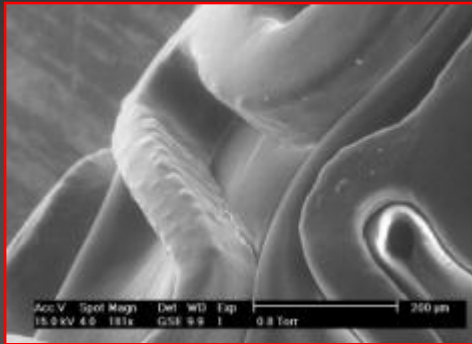
EPITOME I

# The 3 Components of DES

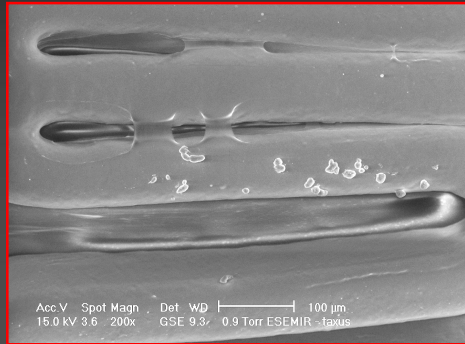


# Current Problems with Polymers

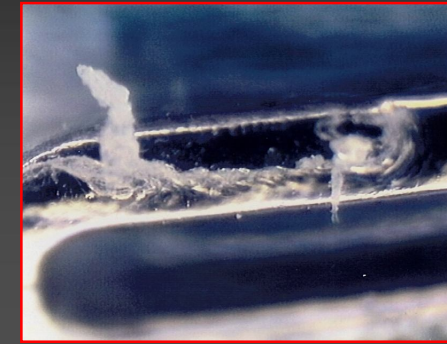
Shortcomings often associated with polymers during stent delivery



Non uniform polymer coating



“Webbed” polymer surface leading to stent expansion issues”

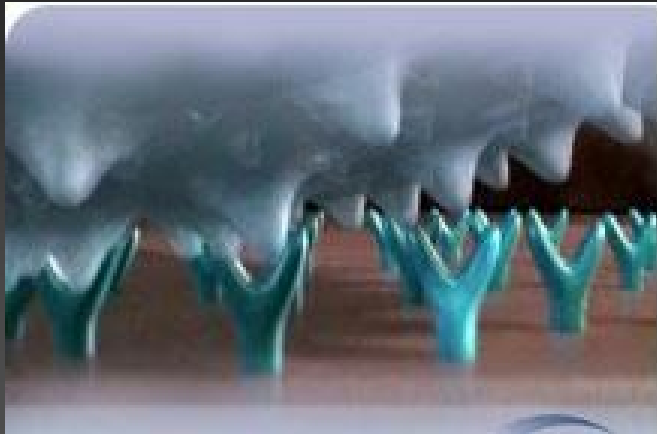


Polymer delamination

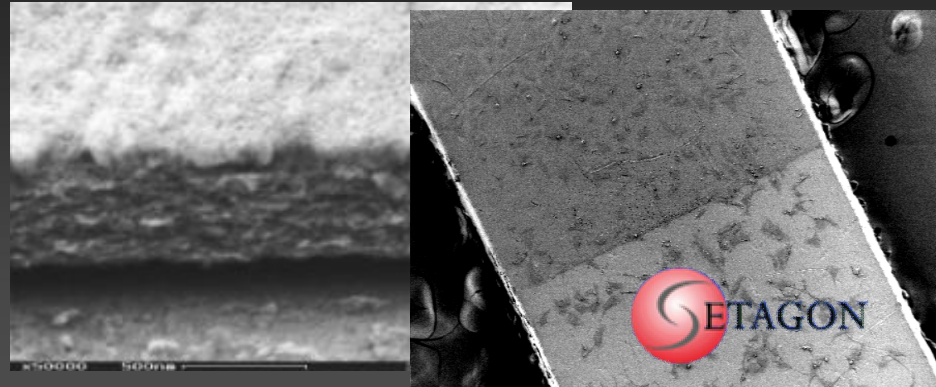
- Durable Coatings-Potential for:
  - Continuing source of inflammation
  - Poor healing/thrombosis risk

# Surfaces to Encourage Cell Growth

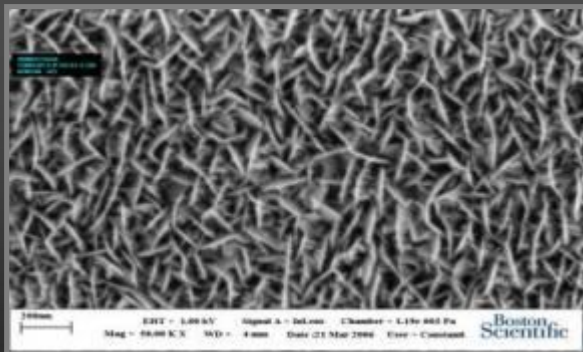
*Bioactive surfaces to accelerate functional endothelialization*



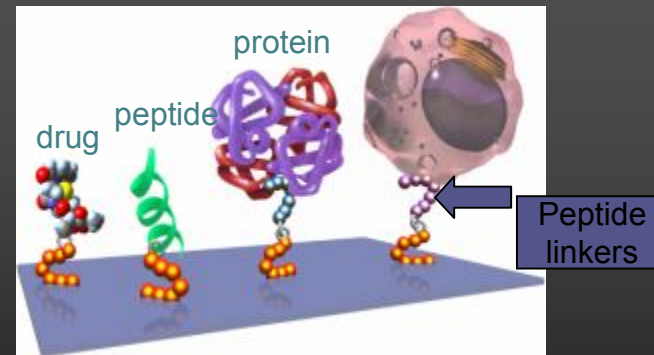
Orbus – EPC Capture



Nanotextured Surfaces  
cell



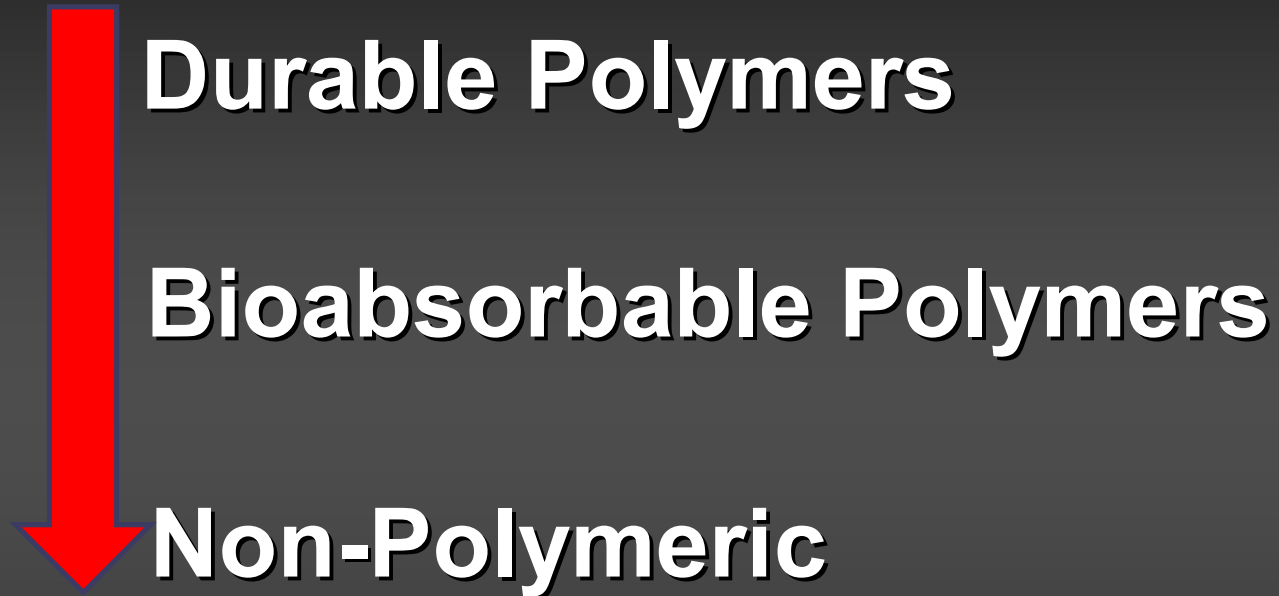
Example of IrOx



device surface

Cell specific peptide linkers (Affinergy)

# Polymer Evolution



# Polymer Evolution



Durable Polymers

Bioabsorbable Polymers

Non-Polymeric

# The NEVO™ Polymer

- **Fully bioresorbable PLGA polymer (exclusively housed in reservoirs):**
- **Benefits**
  - Complete resorption in 3-4 months
  - Fully metabolized
  - Highly biocompatible and hemocompatible
  - Future applications could use different comonomer ratios to permit variable resorption times (few weeks-many months)



# The Res-Elution I Trial - Overview

## Study design and Follow-up

Single De Novo Native Coronary Artery Lesions  
Reference Vessel Diameter: 2.5 - 3.5 mm  
Lesion Length:  $\leq 28$  mm  
Pre-dilatation Required

40 sites worldwide:  
Europe, South America, Australia and New Zealand  
388 subjects randomized 1:1

Principal Investigators:

Christian Spaulding,  
John Ormiston,  
Alexandre Abizaid

**NEVO™ Arm**  
n = 194 subjects

**Taxus® Liberté™ Arm\***  
n = 194 subjects

Primary Endpoint: 6 mo in-stent late loss  
Sub-Study: IVUS subset (50 subjects per arm)  
Dual antiplatelet therapy for 6 mo. minimum

Clinical/ MACE

30 Day

6 Mo.

1 Yr.

2 Yr.

3 Yr.

4 Yr.

5 Yr.

Angiographic/ IVUS

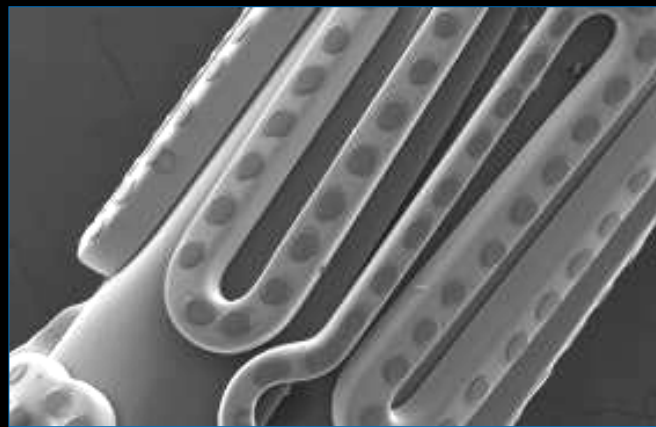
\*The third party marks used herein are trademarks of their respective owners.



# JACTAX Stent Technology (Labcoat, Ltd)

Bioerodable, abluminal coating

- Droplets of polymer-drug coating on the outside surface of the stent only
- Reduced amount of drug and polymer
- BMS surface on three sides
- Drug only where required



# JACTAX Trial

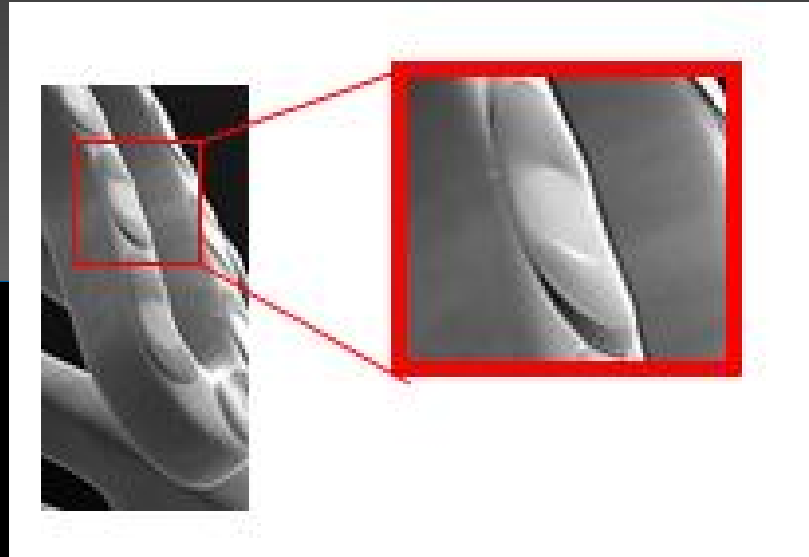
PI: Eberhard Grube

## Stent Platform

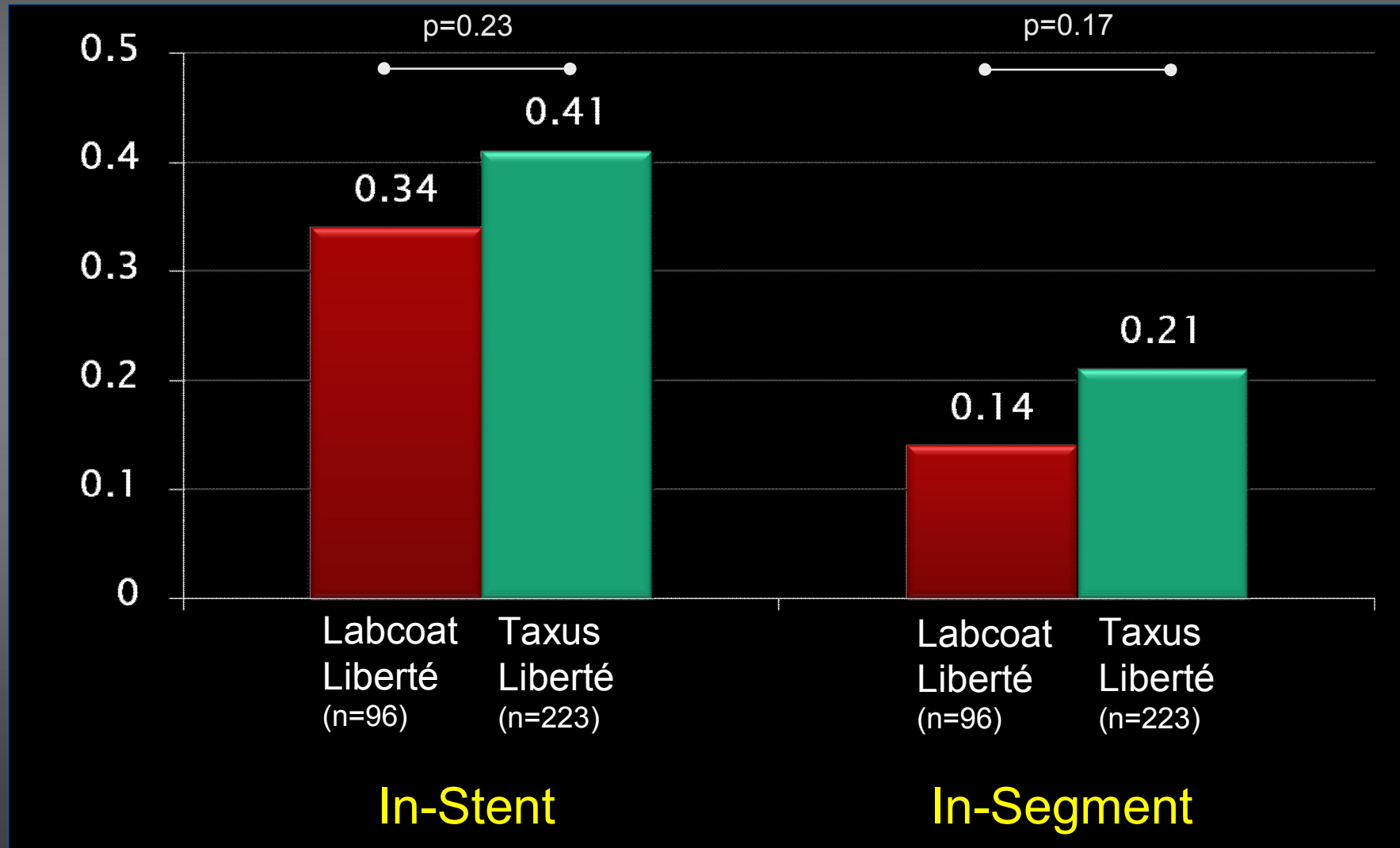
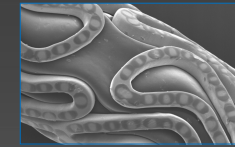
- Liberté<sup>®</sup> Pre-mounted stent (BSC)

## JA<sup>®</sup> Coating

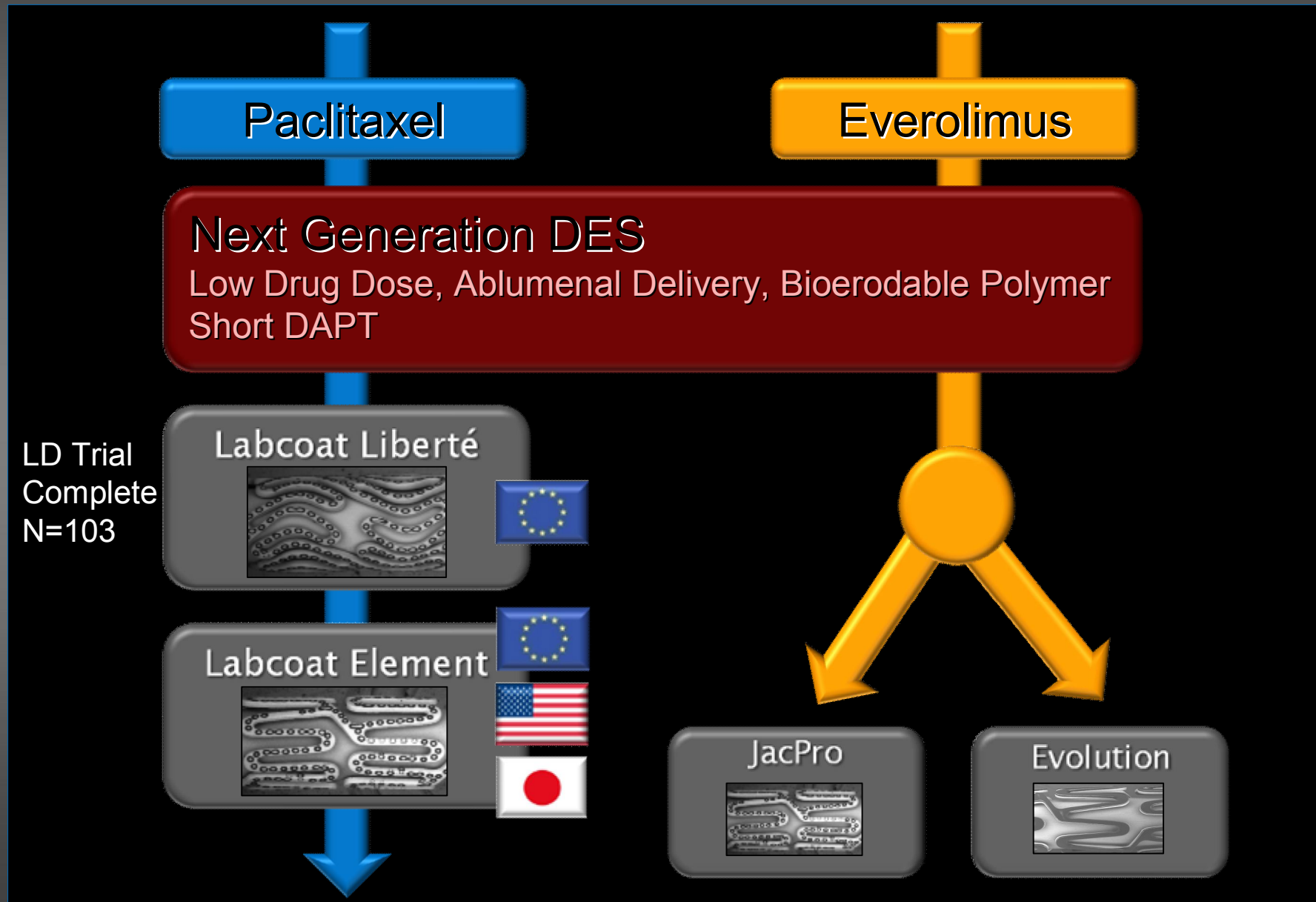
- 9.2 µg. of Paclitaxel and 9.2 µg. DLPLA (16 mm)
- 2700 microdots (16 mm)
- Mass of polymer approx 3.4 ng. per microdot
- < 1 micron thick, abluminal and low molecular weight biodegradable polymer decreases persistence time



# JACTAX HD Results vs. ATLAS Matched (9 months)



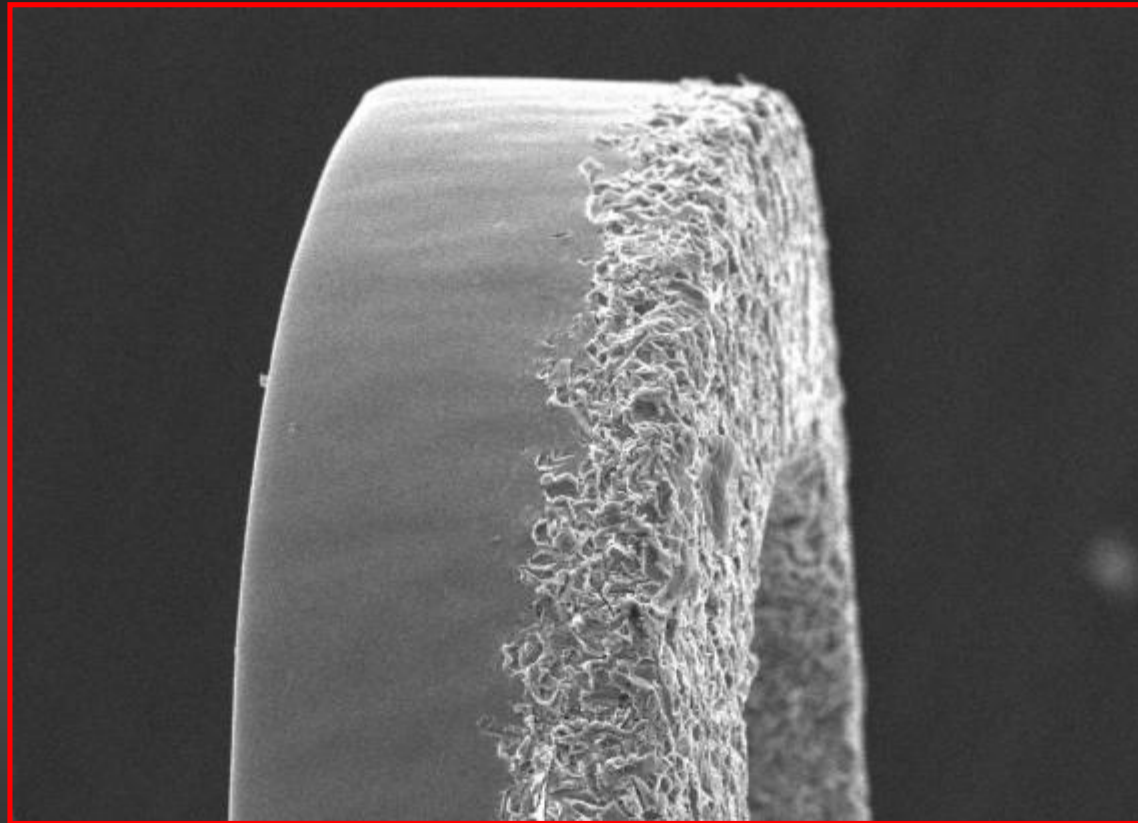
# BSC Two Drug Strategy



**Better than any polymer is no polymer...**

# BioMatrix Freedom Stent

## Micro-structured Surface

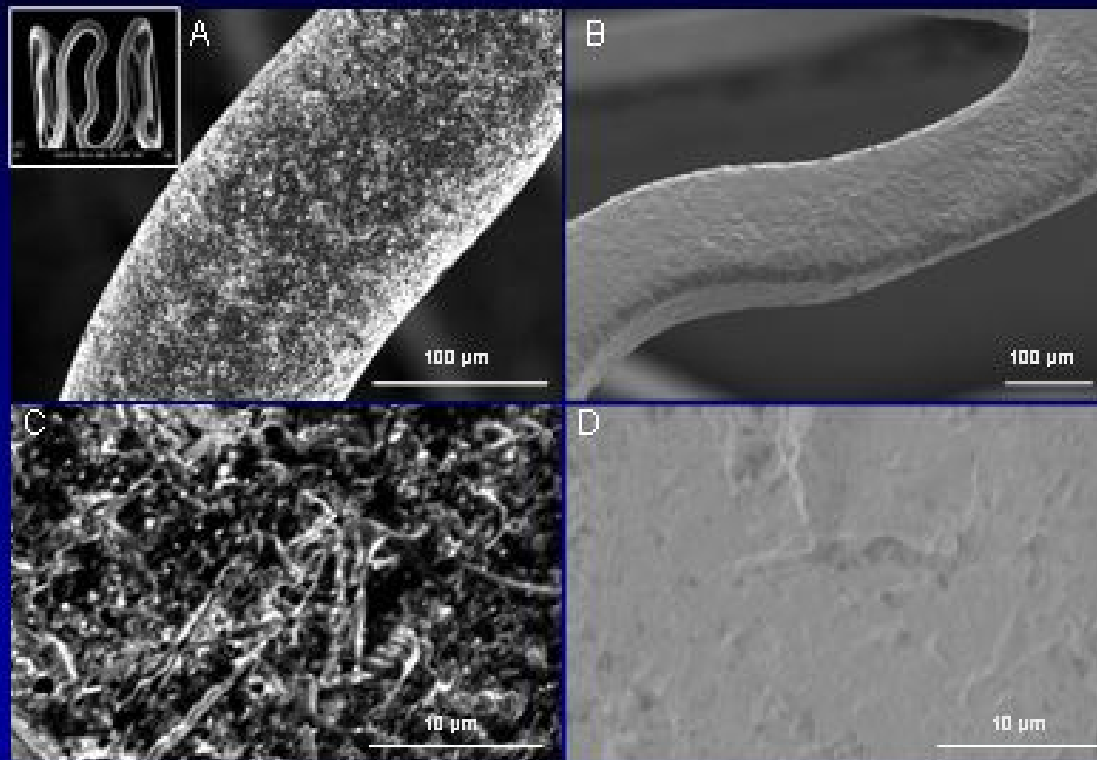


- **Selectively micro-structured surface holds drug in abluminal surface structures**

# Translumina Porous Surface Stent



## Unique microporous stent surface



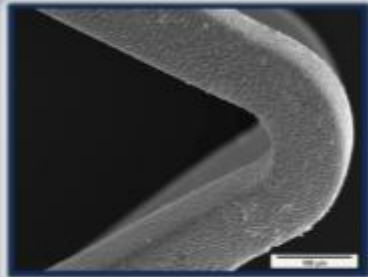
before

coating

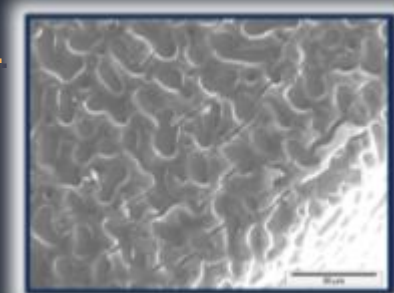
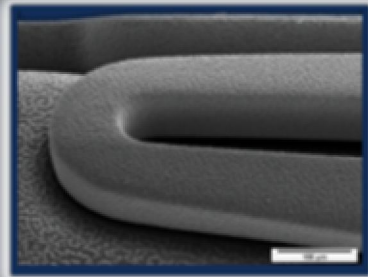
after

Pure  
Sirolimus

# Polymer Free Paclitaxel

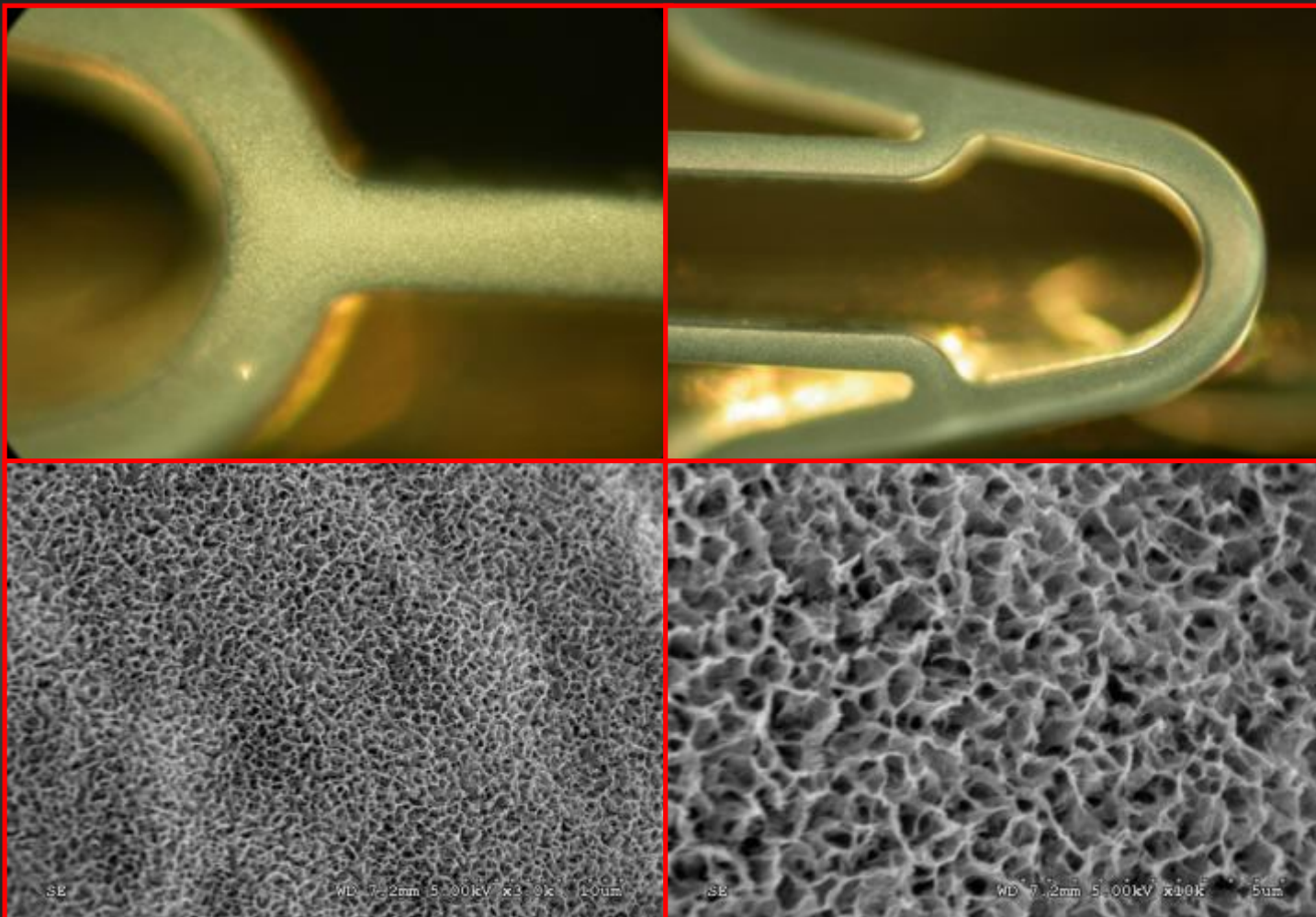


- Abluminal coating – 5 $\mu$  thickness applied on crimped stent.
- Consistent coating ensuring 98% of the drug delivered to the site.
- Polymer free Paclitaxel.
- 2.5 $\mu$ g/mm<sup>2</sup> dose.
- Boost-release (60% in 2 days)
- Profile release established in 30 days (98% of the drug)
- Back to regular Chromium Cobalt after 45 days.





# 3D MicroPorous Nanofilm HAp



# QCA Results Follow-up

Variable	4 months (n=15)		9 months (n=12)	
	In-Stent	In-Lesion	In-Stent	In-Lesion
MLD, mm	2.34 ± 0.33	2.05 ± 0.38	2.27 ± 0.33	2.02 ± 0.29
% Diameter stenosis	13.8 ± 7.0	23.6 ± 8.8	15.9 ± 8.20	23.6 ± 9.50
Late lumen loss, mm	<b>0.29 ± 0.25</b>	0.16 ± 0.29	<b>0.36 ± 0.24</b>	0.20 ± 0.31
Restenosis*, % (n)	0	0	0	0

Abizaid et al. ACC 2008.

# IVUS Volumetric Analysis

## Baseline / 4 month / 9 month follow-up

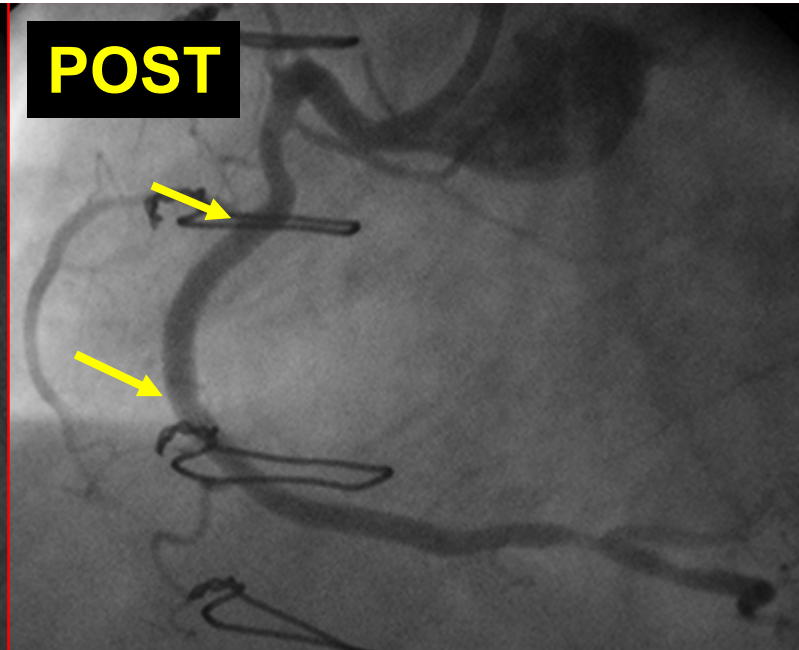
IVUS variables	Baseline N= 14 P*	4-month follow-up N= 14 P*	9-month follow-up N= 14 P*
Vessel Volume (mm <sup>3</sup> )	294.2 ± 117.1	286.9 ± 87.4	296.8 ± 85.6
Stent Volume (mm <sup>3</sup> )	144.5 ± 48.2	140.5 ± 36.7	143.1 ± 41.4
Lumen Volume (mm <sup>3</sup> )	144.7 ± 48.4	136.3 ± 34.2	136.8 ± 38.2
NIH Volume (mm <sup>3</sup> )	N/A	4.3 ± 3.5	6.1 ± 4.9
Mallaposition Volume (mm <sup>3</sup> )	0.34 ± 0.87	0.14 ± 0.34	0.13 ± 0.36
% Stent Obstruction	N/A	2.8 ± 2.2	3.8 ± 2.3

\* 1 pt refused to undergo invasive FU at 9 months and therefore were excluded from this sub analysis.

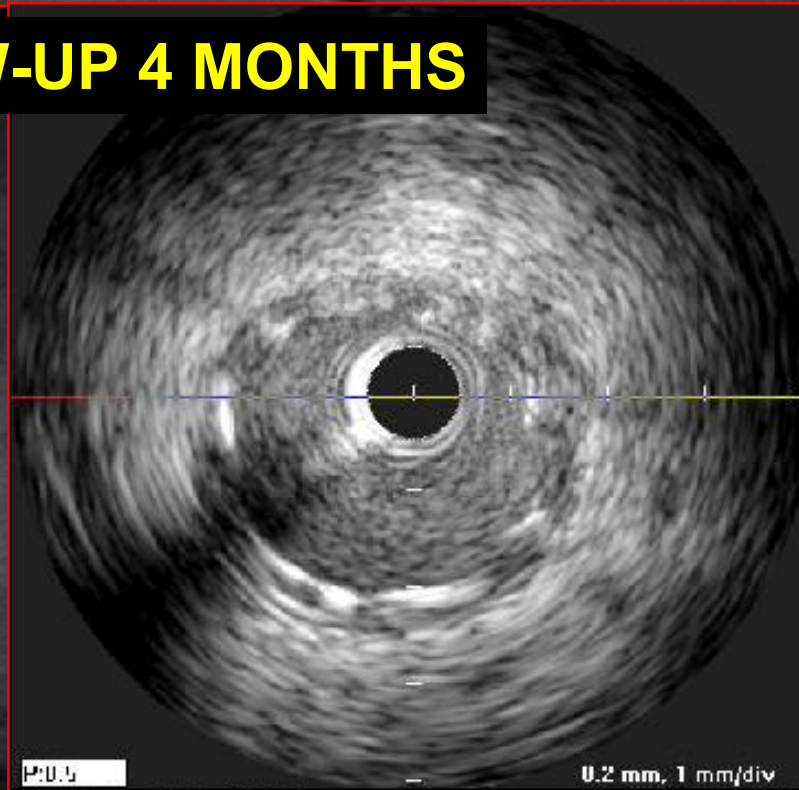
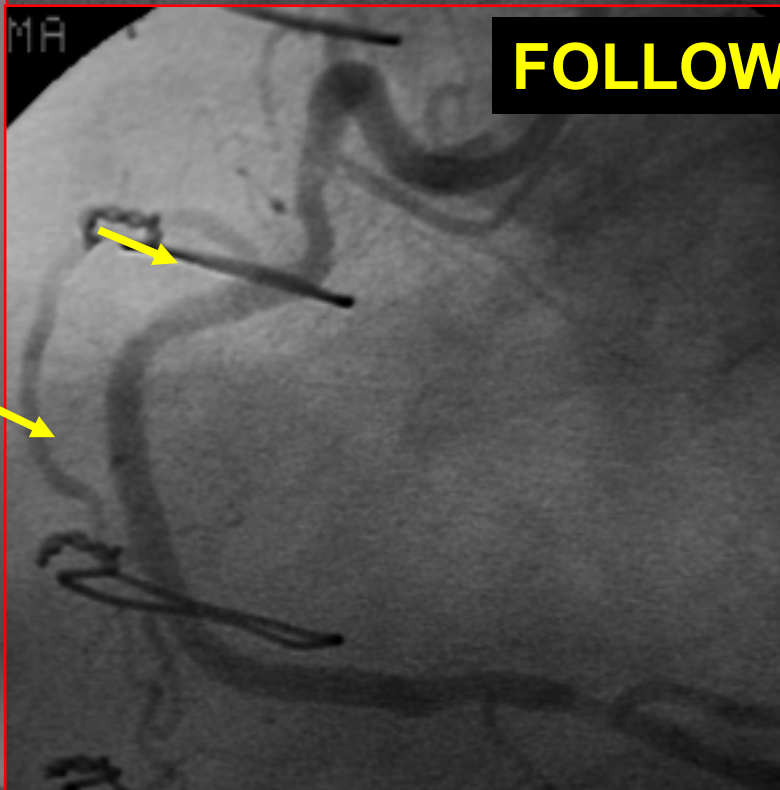
**PRE**



**POST**

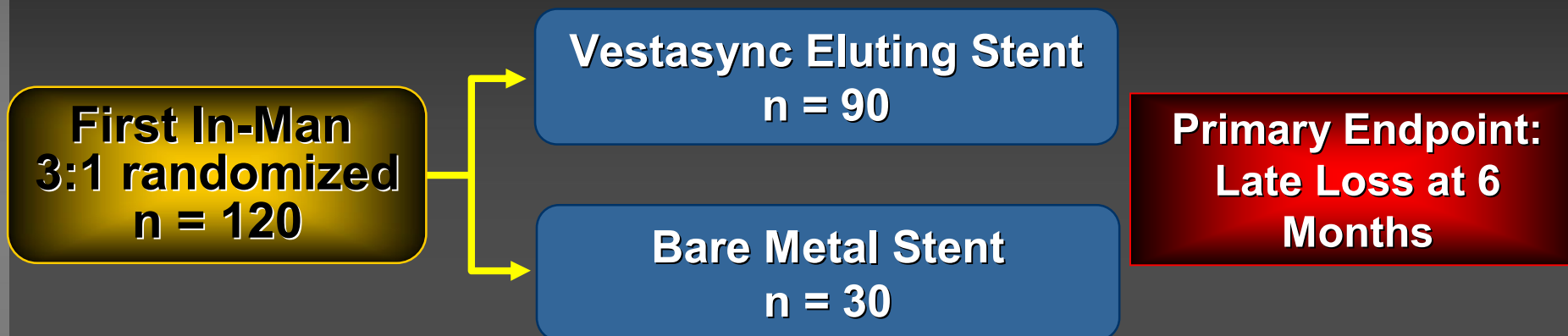


**FOLLOW-UP 4 MONTHS**



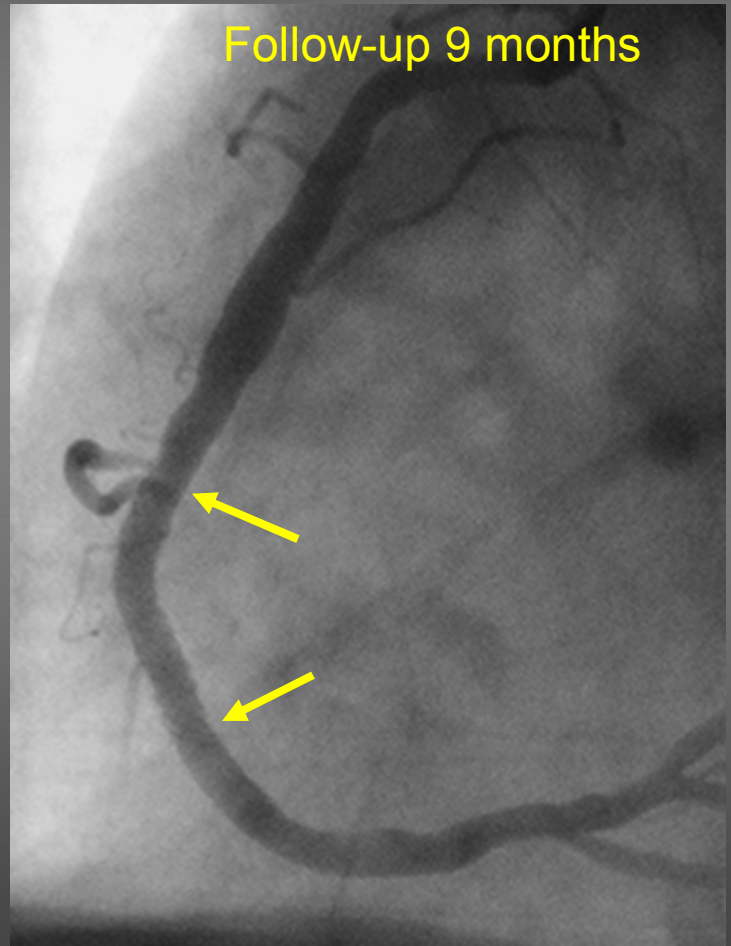
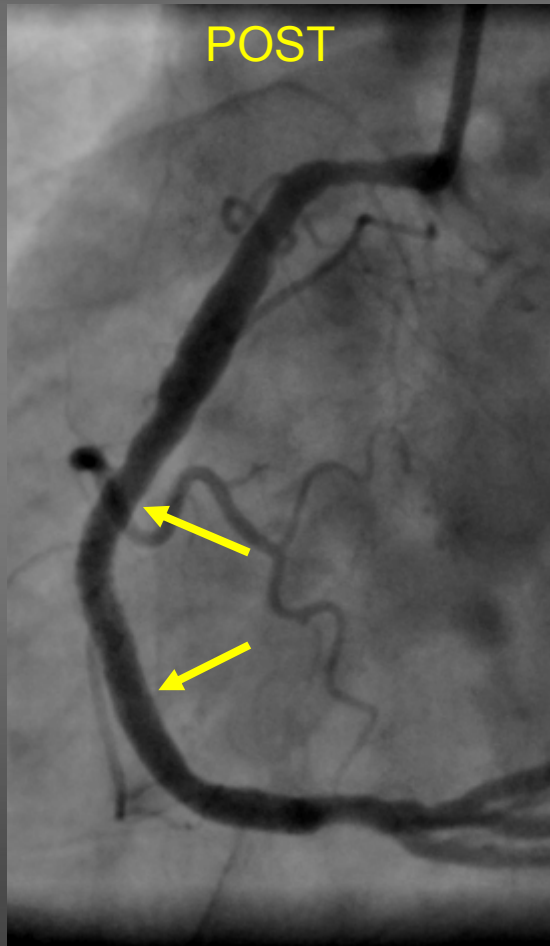
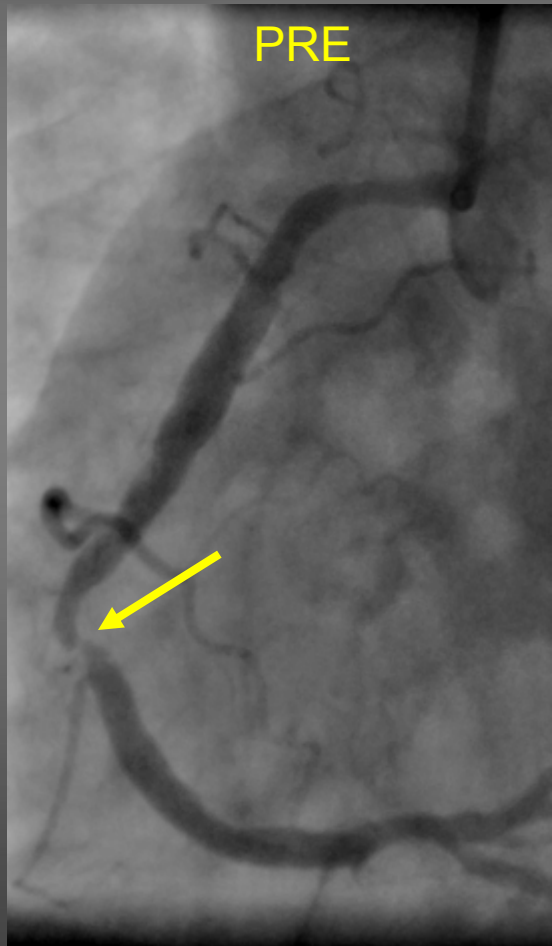
# VESTASYNC II

## Polymer-Free Sirolimus-Eluting Stent



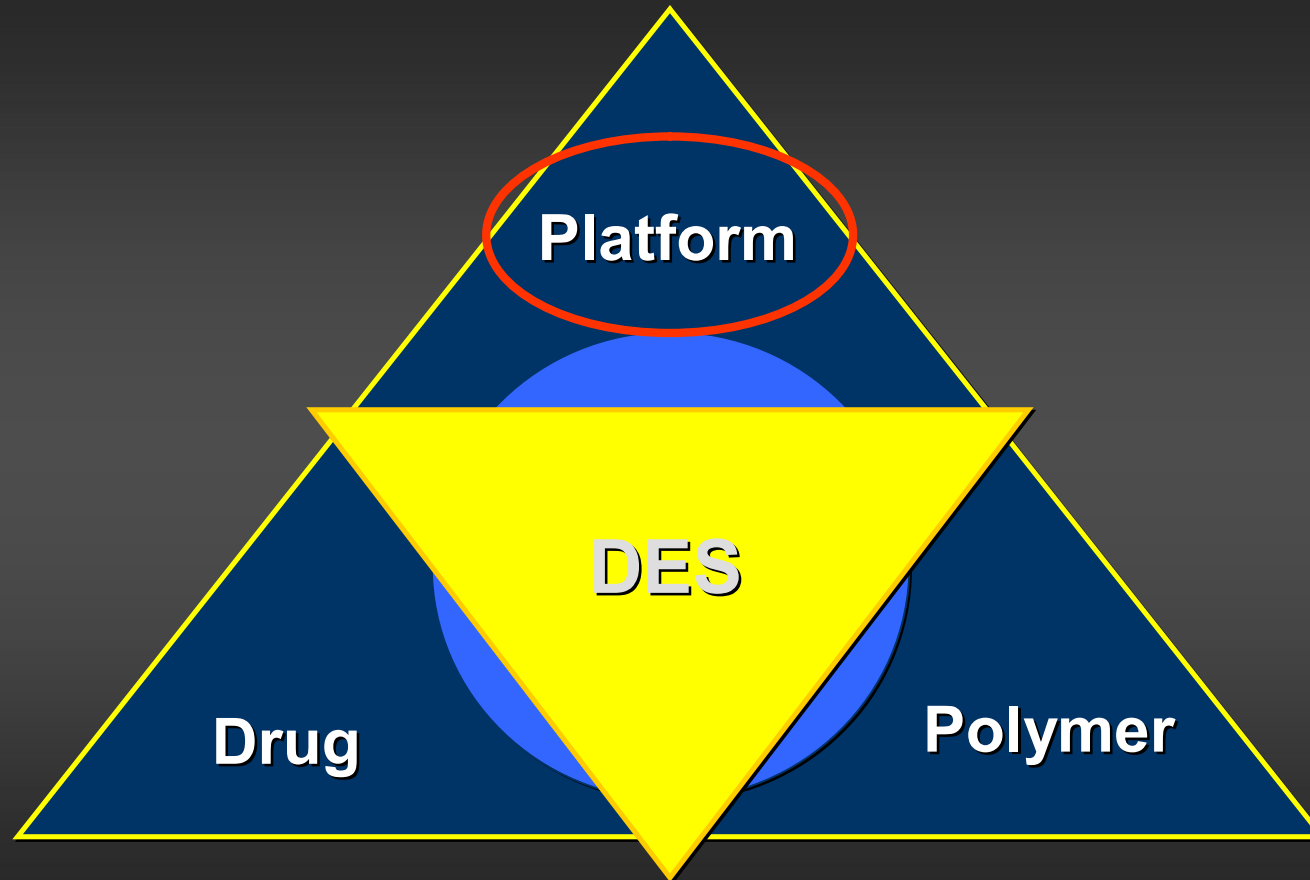
- IVUS subanalysis: 30 pts
- OCT sub-analysis : 30 pts
- Endothelial function: 20 pts



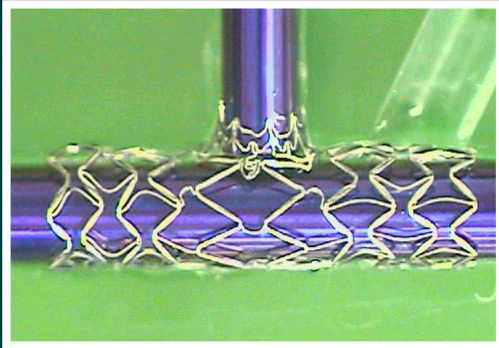


# 10 - 156004 LANB

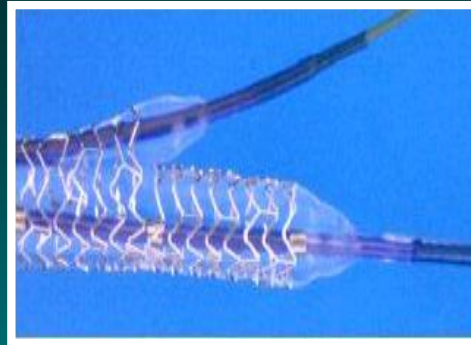
# The 3 Components of DES



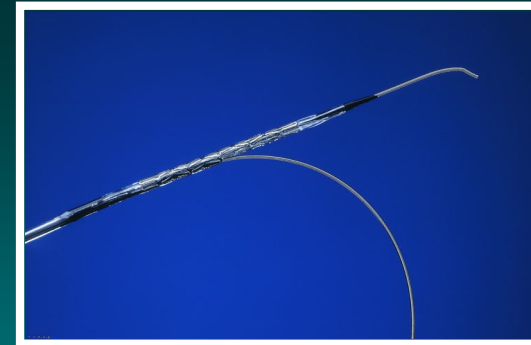
# Dedicated Bifurcation Stents



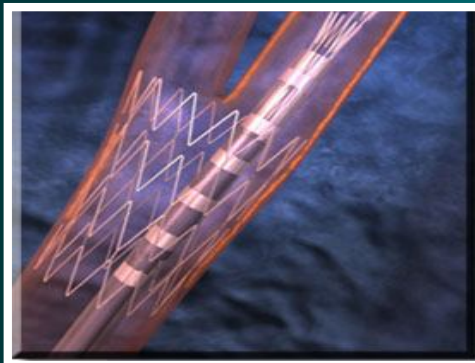
**Taxus petal**



**Abbott pathfinder**



**YMed sidekick**



**Devax (+ BA9)**

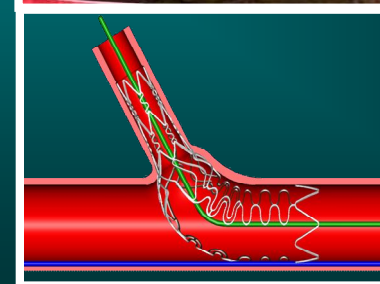


**MDT**  
**"True" bifurcation designs**



**Cappella**

**Side-branch designs**



**Tryton**





# **DIVERGE: Drug Stent Intervention for Treating Side Branches Effectively**

*Prospective, Single-arm, Multicenter Registry*

*Patients with de novo bifurcated lesions in  
native coronary arteries N=300*

**PCI using Axxess™ stent System**

**Angio F/U at 9 mo in 300 pts  
Annual clinical F/U for 5 years**

**PRIMARY Endpoint: 9-mo MACE: death, MI, iTLR**

**SECONDARY Endpoints: device success, binary restenosis, late loss**

# DIVERGE - Clinical Results

## Cumulative 9 Month MACE

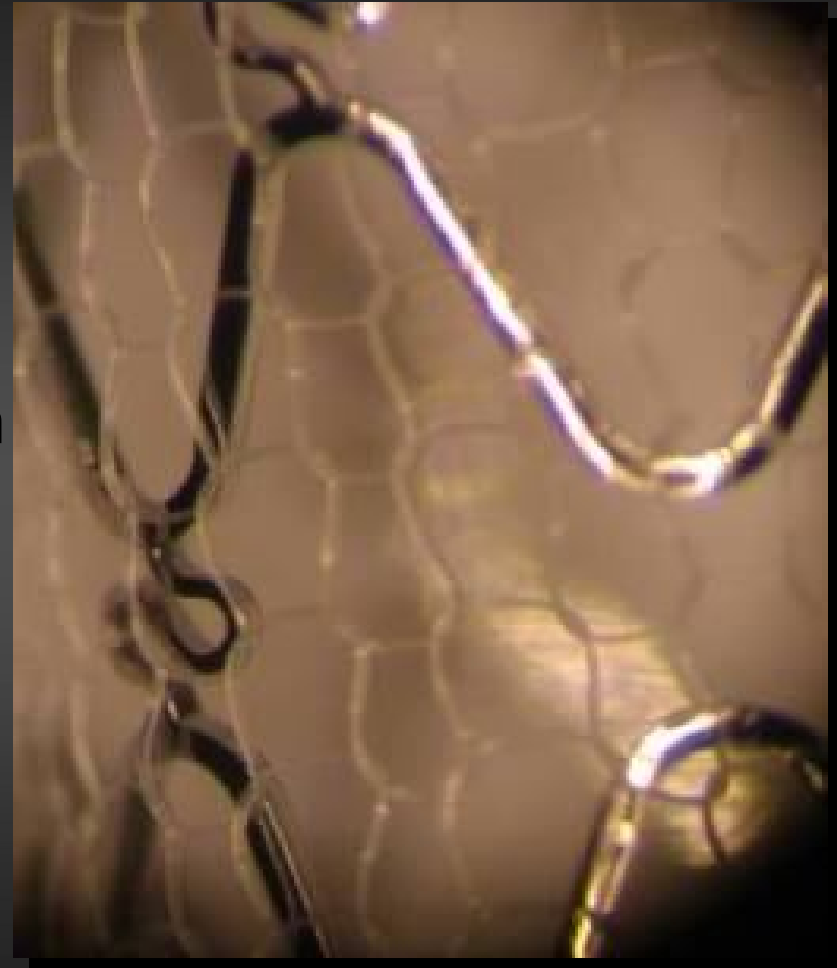
N completing follow up (%)	99.3% (300)
All-cause MACE	7.7%
<i>Any death</i>	0.7%
<i>Q wave MI</i>	1.0%
<i>Non-Q wave MI</i>	3.3%
<i>Ischemia-driven TLR - ALL BIFURCATION</i>	4.3%
<i>Exclusively side branch driven</i>	1.3%

# DIVERGE - 9 Mo QCA Results

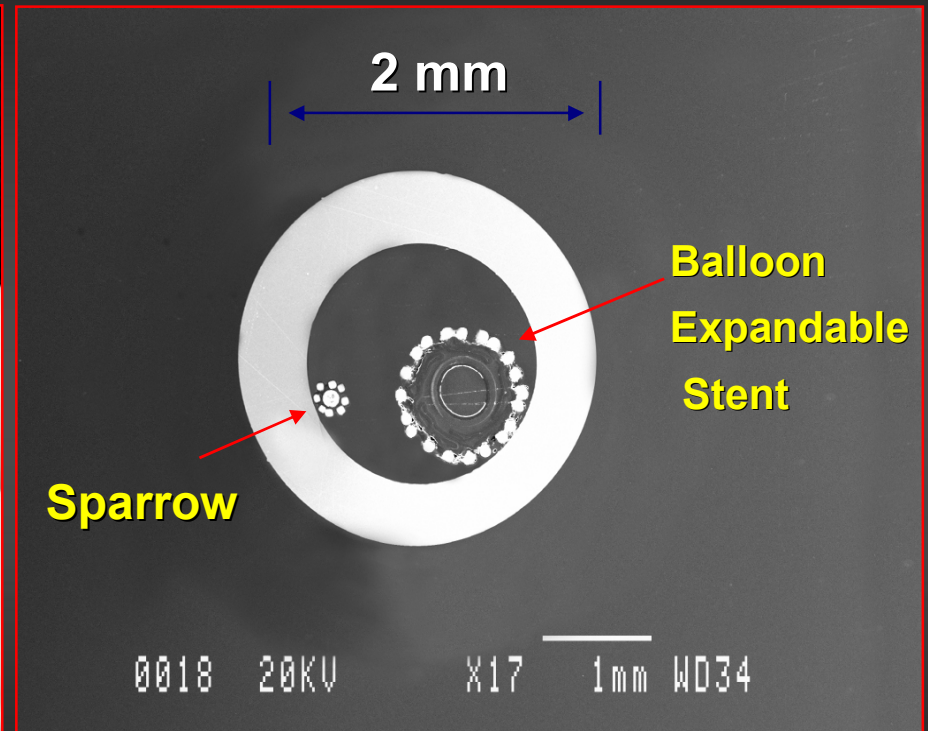
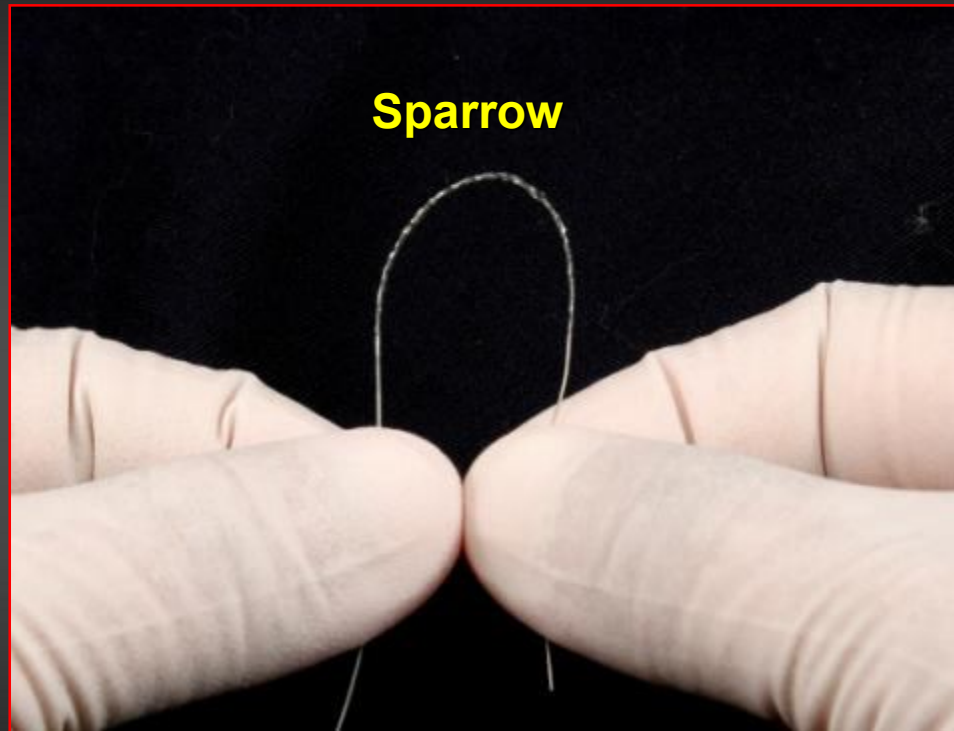
At Follow Up		MV (N=140)	SB (N=140)
Late Loss (mm)	In-stent LL (AXXESS only)	0.18	-
	In-stent LL (all stents)	0.29	0.29
	In-lesion LL	0.20	0.17
Restenosis <i>Per Vessel</i>	In-stent - AXXESS Only	0.7%	--
	In-stent - Cypher	2.3%	4.8%
	In-lesion restenosis (all stents + edges)	3.6%	4.3%
Overall	In-stent - PV + SB	5.0% (7/140)	
Bifurcation Restenosis	In-stent or edges, within PV + SB	6.4% (9/140)	

# What is the MGuard Stent?

**A stent wrapped with ultra-thin polymer mesh sleeve, knitted to the external surface**



# The CardioMind Sparrow™: Stent on a .014" Guide Wire Platform



# CARE I

## 6 Month QCA Results

Characteristic	Aggregate (n=20)
In-stent % DS	38.12 $\pm$ 26.77
In-segment % DS	39.87 $\pm$ 24.51
In-stent MLD (mm)	1.35 $\pm$ 0.60
In-segment MLD (mm)	1.31 $\pm$ 0.54
<b>In-stent LLL (mm)</b>	<b>0.73<math>\pm</math>0.57</b>
In-segment LLL (mm)	0.61 $\pm$ 0.51
Binary Restenosis	20% (4/20)



# Future DES....

- Safer **drugs**, lower doses, and combination therapies (anti-proliferative + pro-healing).
- New **polymeric** materials and/or surface modifications will reduce the use of durable polymers.
- **Platforms** customized and designed to treat special anatomic situations (bifurcations, small vessels, SVG, multivessel disease).