Solaci 2012

Update on the Current Status of Enduring DES

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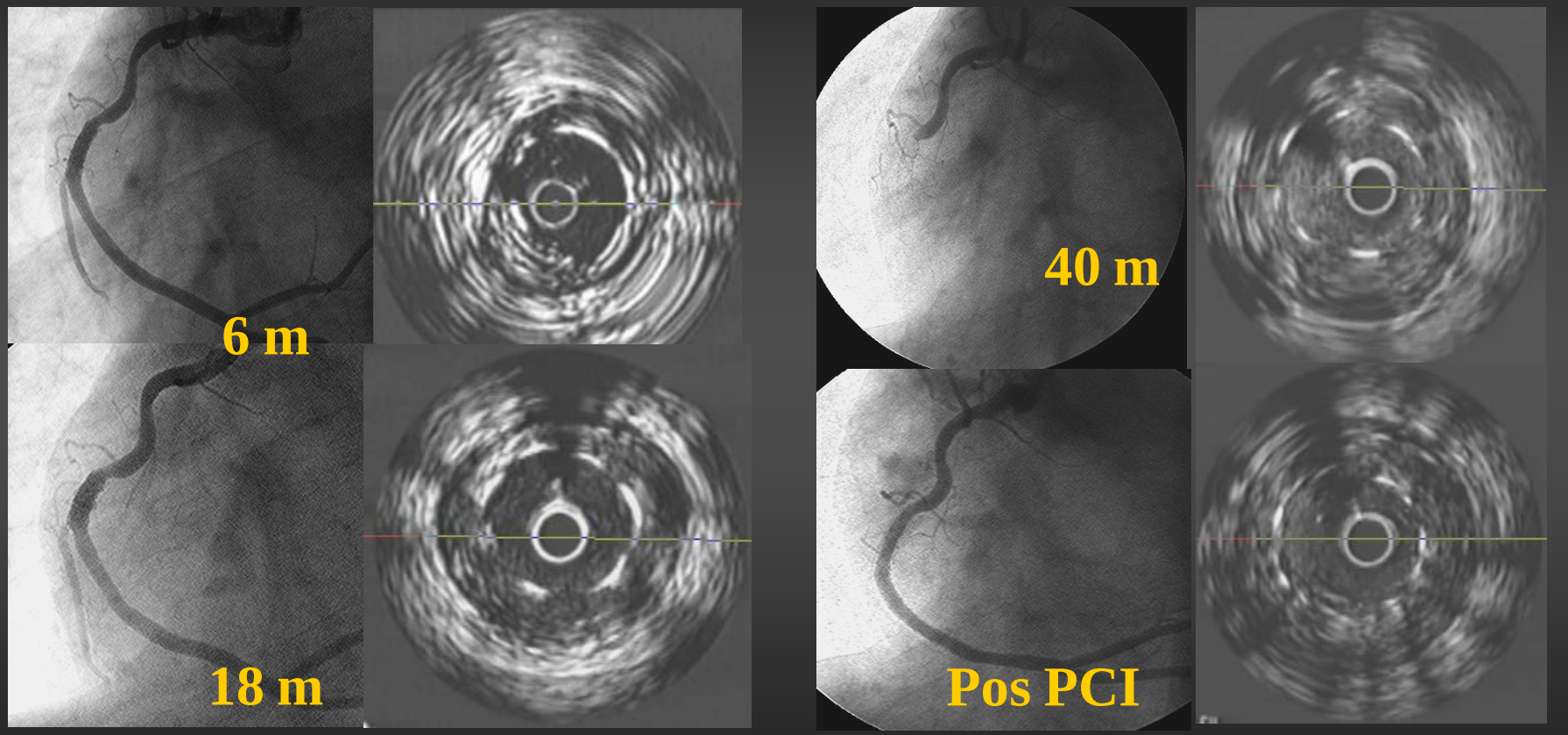
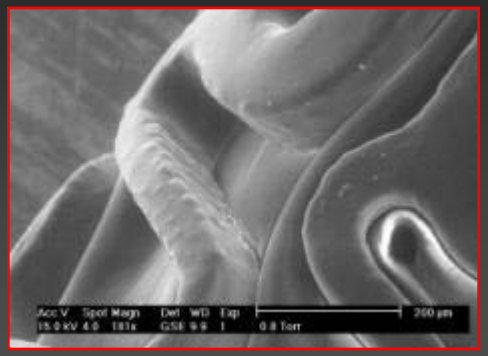
New York, USA

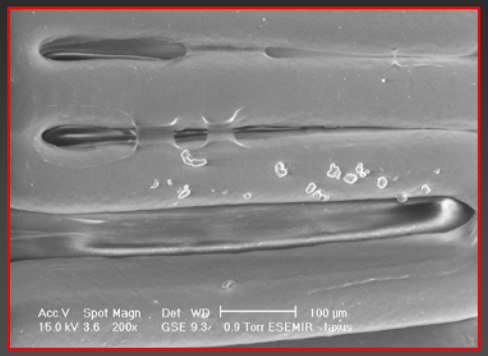
Trombose Tardia com Revascularização do Vaso-alvo



Problemas associados aos polímeros de primeira geração durante a liberação do stent



Distribuição não uniforme



Aprisionamento das hastes levando a má expansão do stent

Delaminação do plímero

- Polímeros duráveis podem ser:
  - Fonte contínua de inflamação
  - Retardo na endotelização
  - Risco de trombose

DES Evolution

Durable Polymers

Bioabsorbable Polymers

Non-polymeric

Bioabsorbable Scaffold

DES Evolution

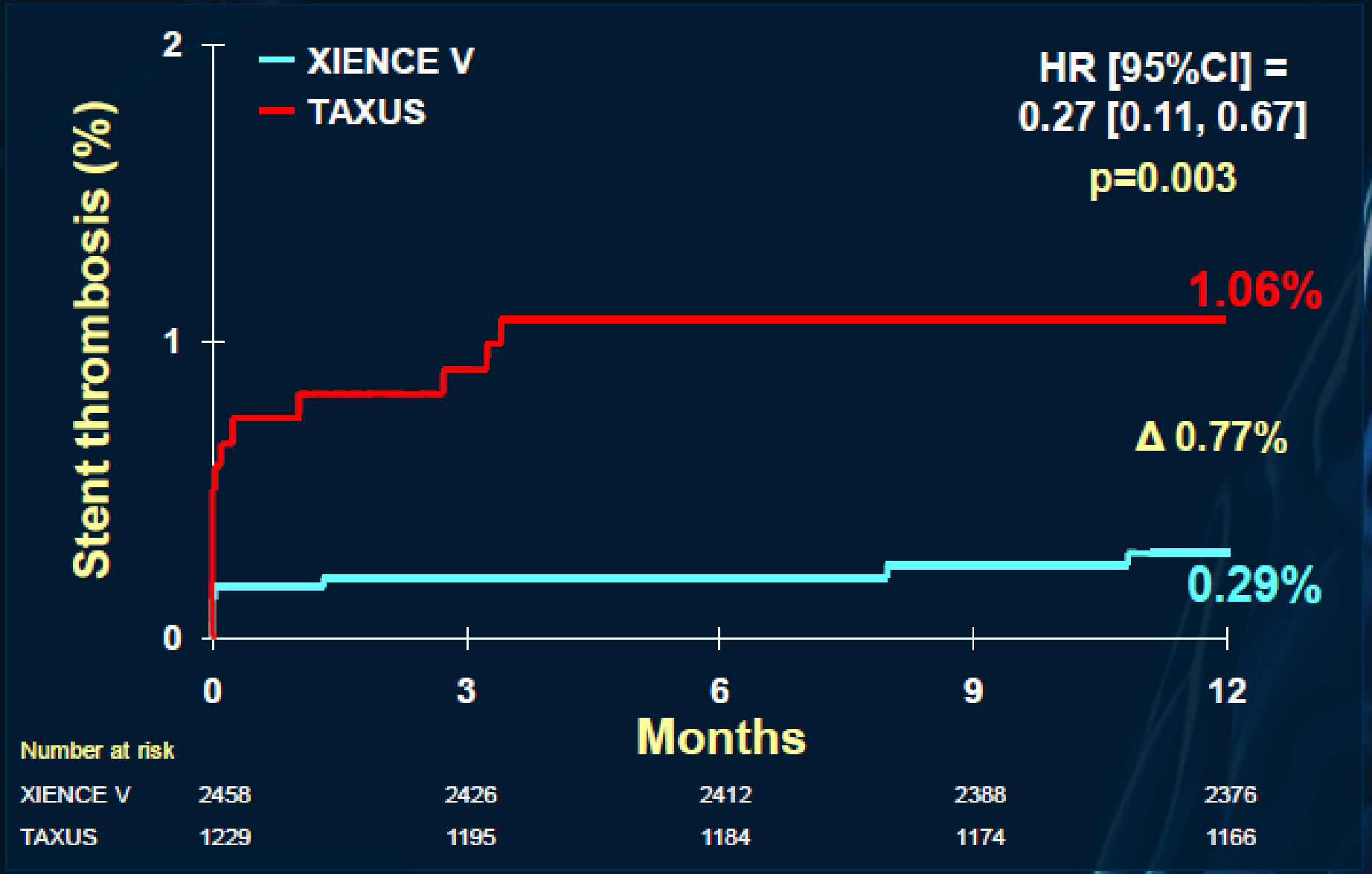
Durable Polymers

Bioabsorbable Polymers

Non-polymeric

Bioabsorbable Scaffold

Stent Thrombosis (ARC Def or Prob)



DES Evolution

Durable Polymers

Bioabsorbable Polymers

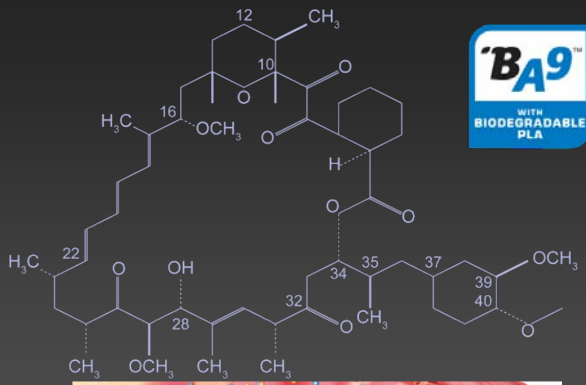
Non-polymeric

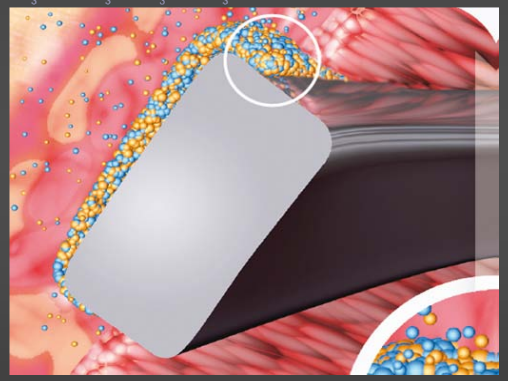
Bioabsorbable Scaffold

DES with Bioabsorbable Polymers

- BioMatrix (Biosensors)
- Synergy (Boston Scientific)
- DESyne (Elixir)
- Inspiron (Scitech)
- Sirolimus + EPC capture (Orbus)
- Biomime (Merril Life Science)

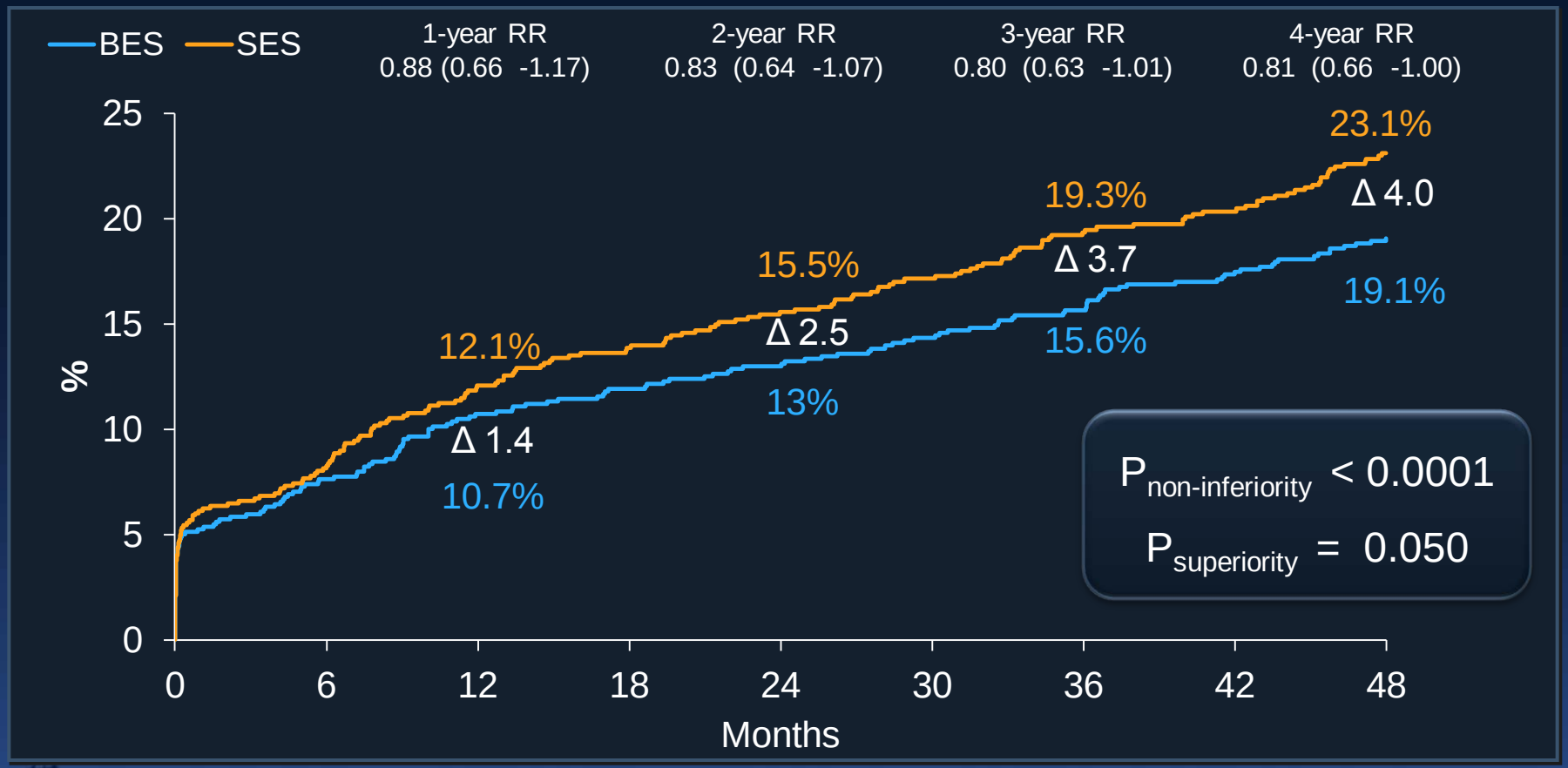
BioMatrix Flex™ DES





- Biolimus is a semi-synthetic sirolimus analogue with **10x higher lipophilicity** and similar potency as sirolimus.
- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to **the abluminal stent surface** by a fully automated process.
- Biolimus is co-released with polylactic acid and completely desolves into carbon dioxide and water after a **6-9 months period**.
- The stainless steel stent platform has a strut thickness of 120 μm with a quadrature link design.

Eventos Cardiacos aos 4 anos

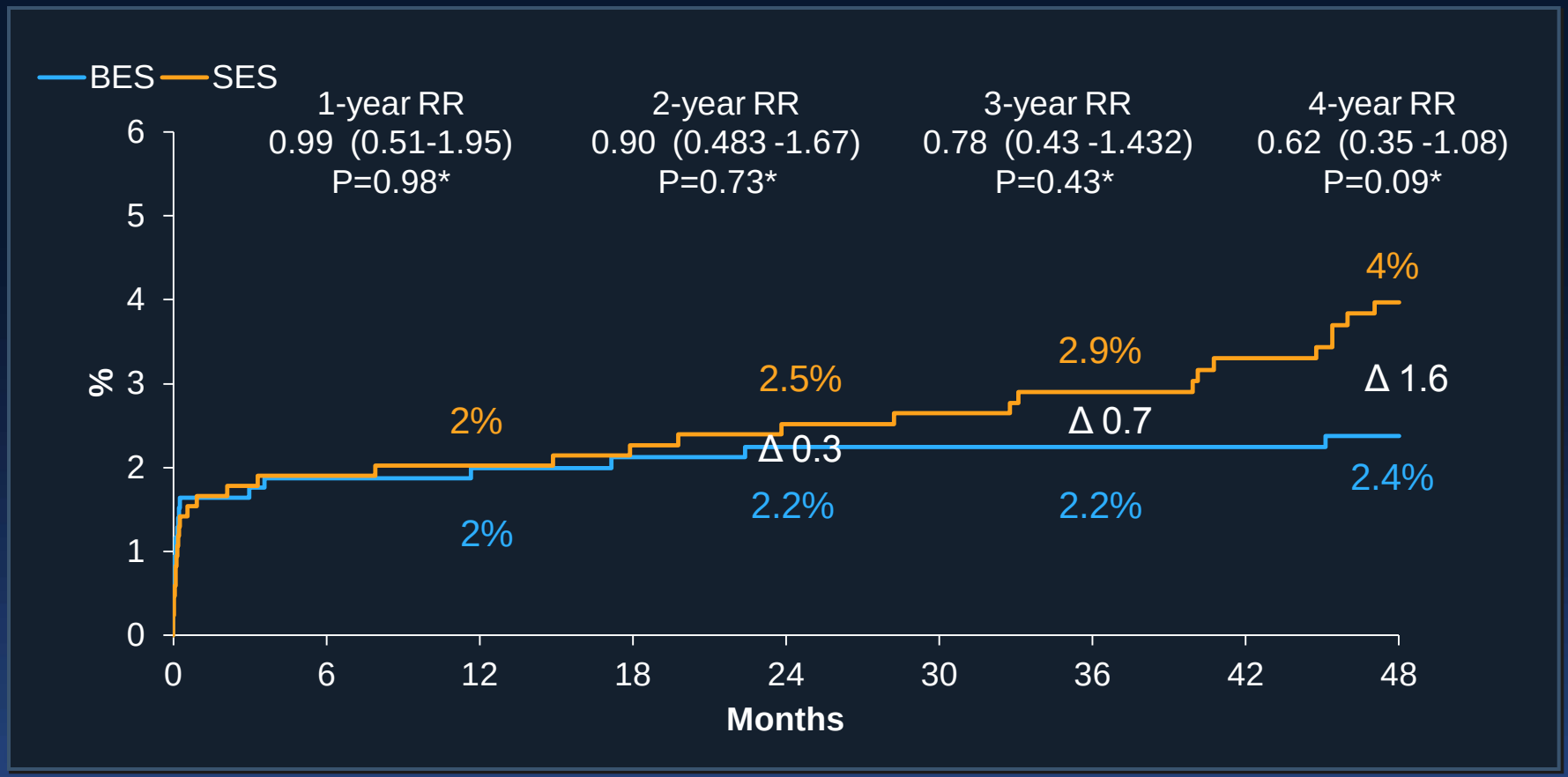


Numbers at risk

SES	850	775	738	718	702	676	656	639	614
BES	857	781	749	733	723	710	697	677	659

MACE = Cardiac death, MI, or Clinically-indicated TVR

Trombose definitiva (ARC) aos 4 anos

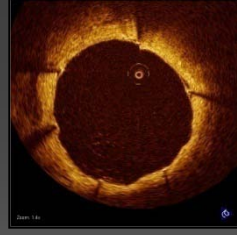


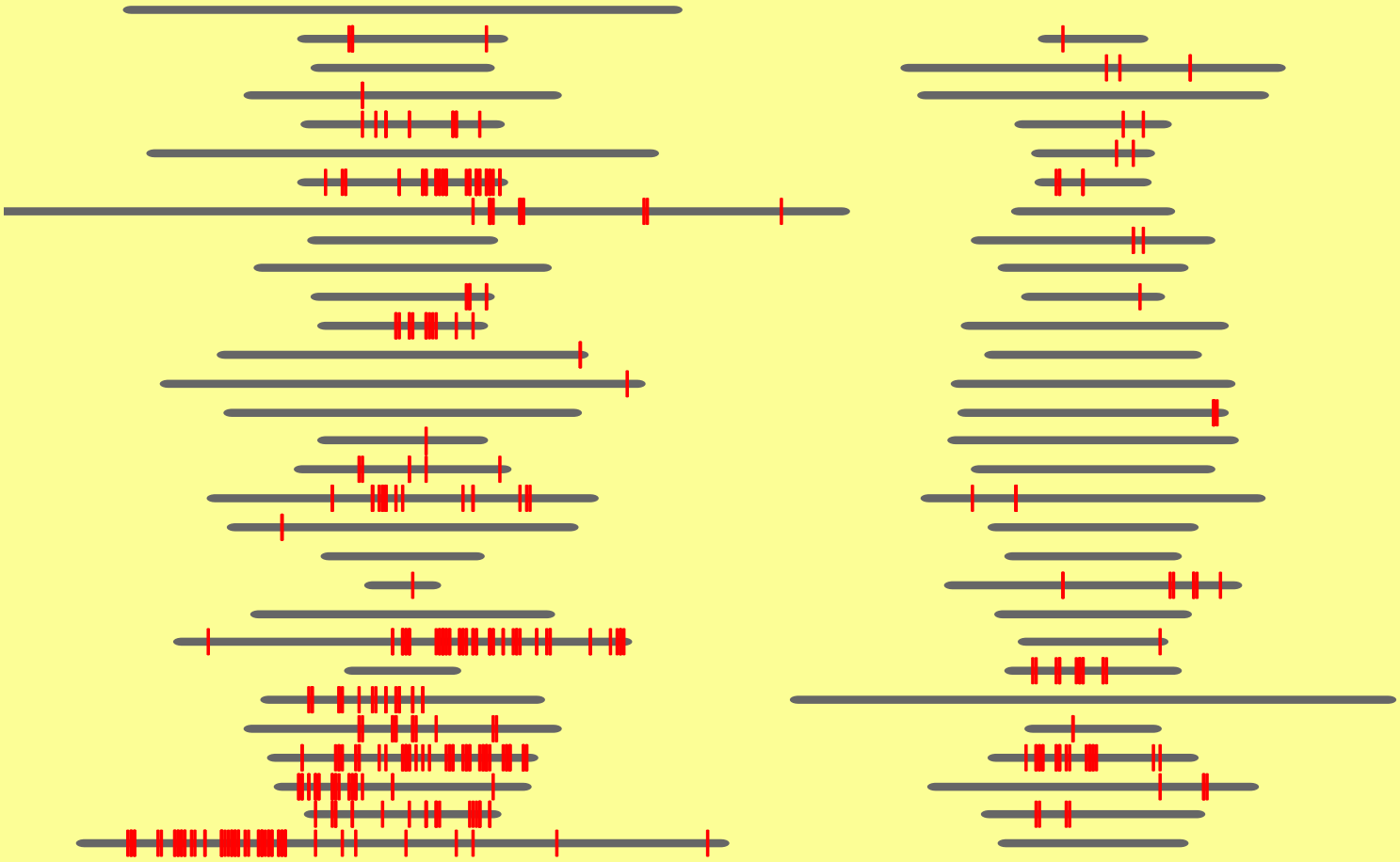
Numbers at risk

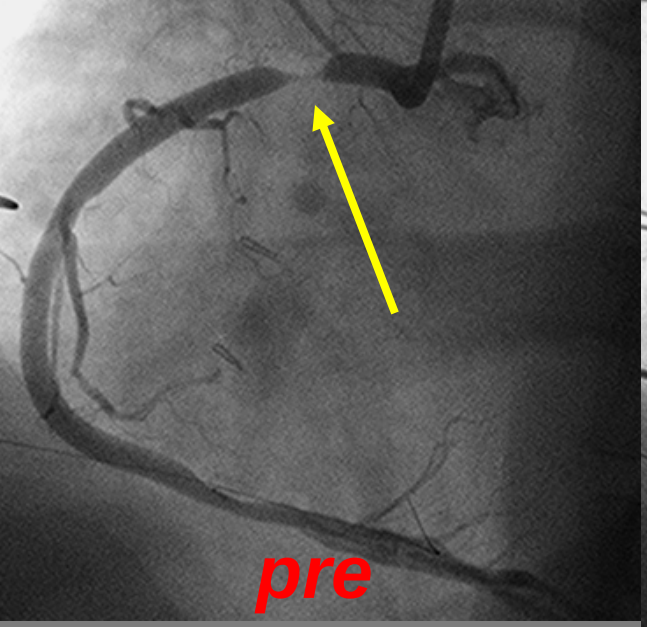
SES	850	817	801	787	776	759	750	730	714
BES	857	821	804	792	787	780	774	757	746

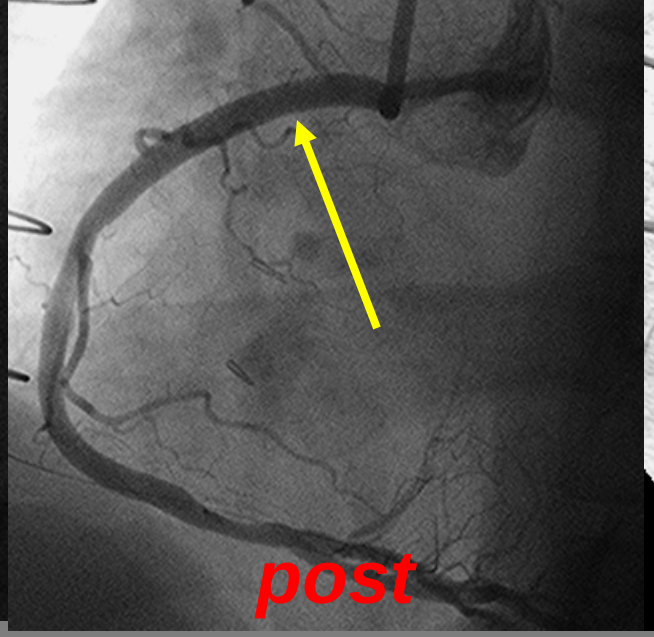
* P values for superiority

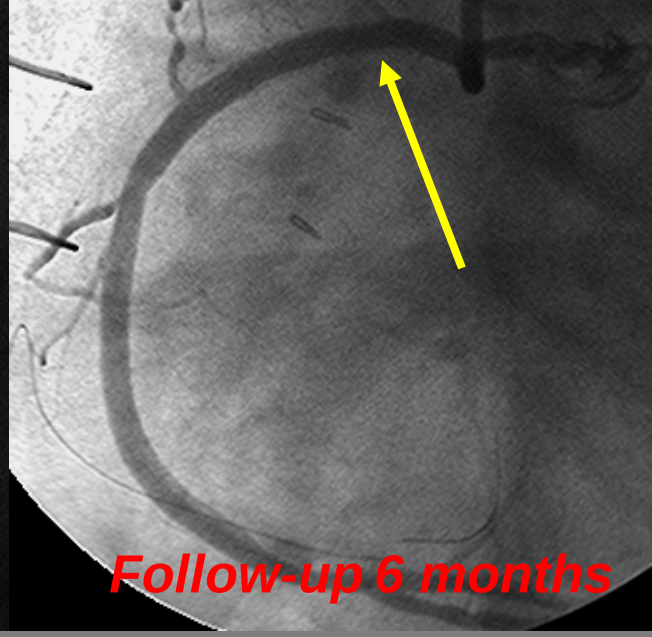
Distribution of Uncovered Struts within Lesions

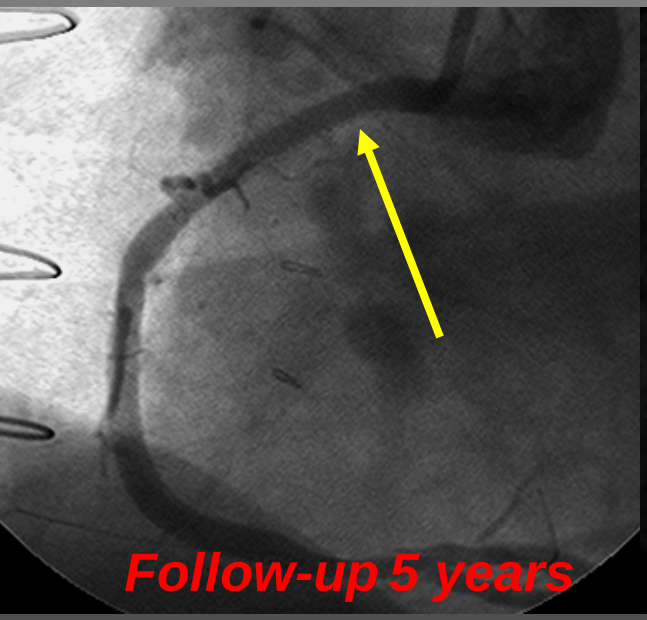


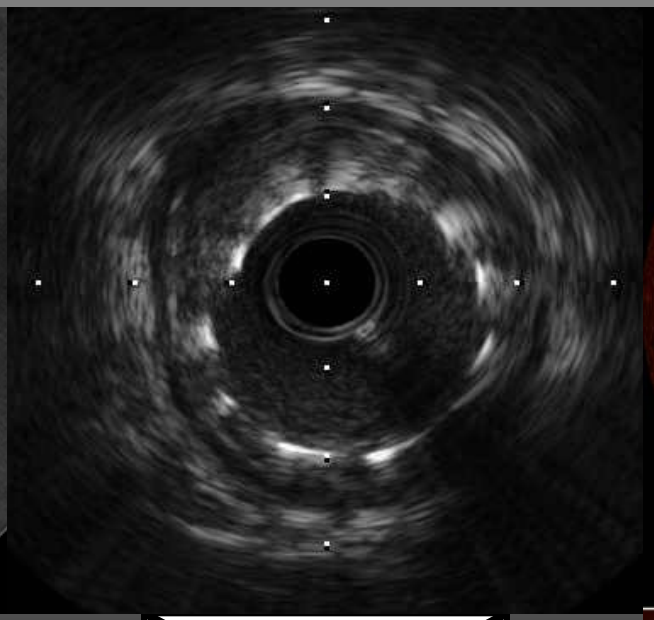


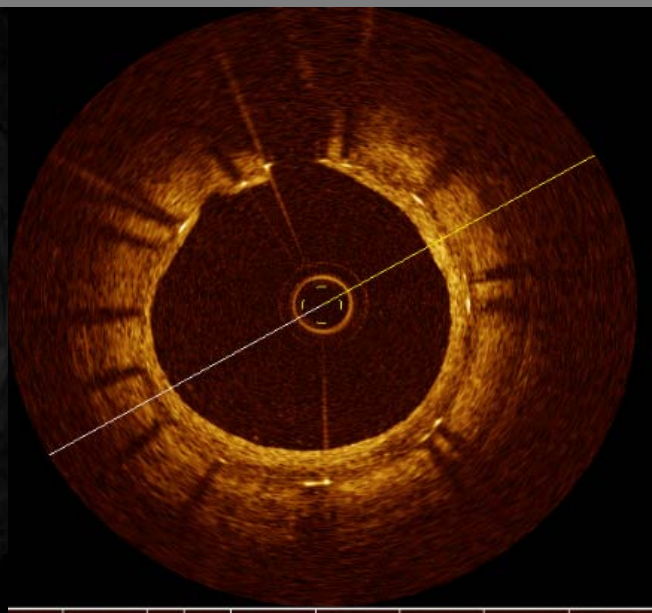






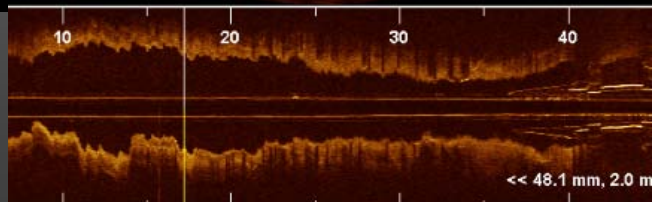


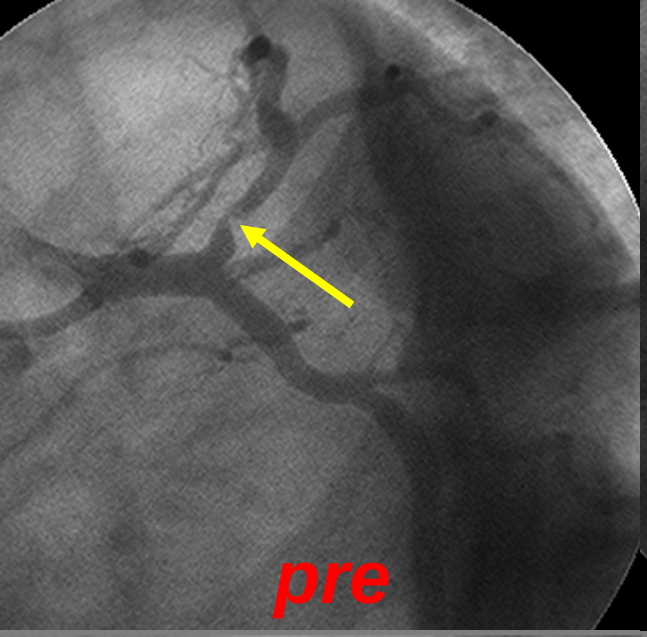


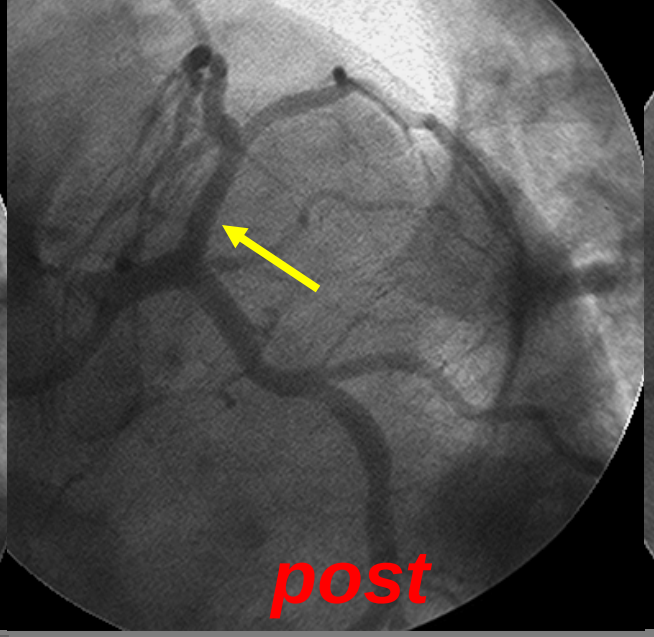


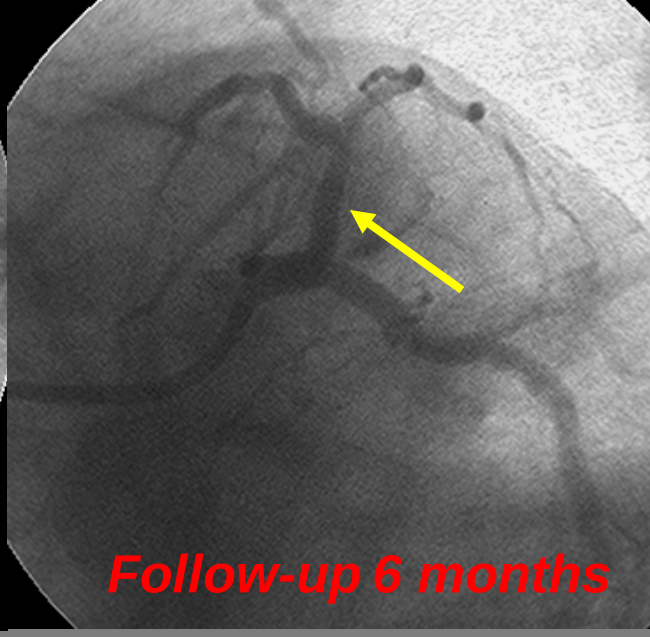
BIOLIMUS-STEALTH

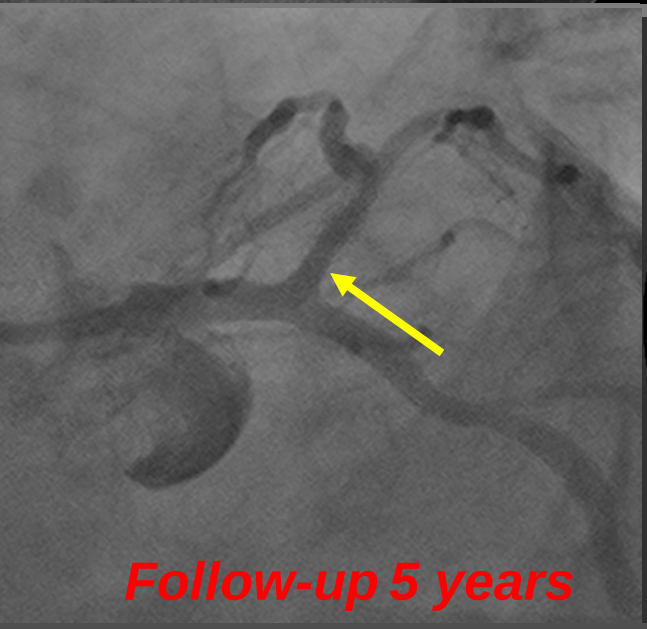
randomization

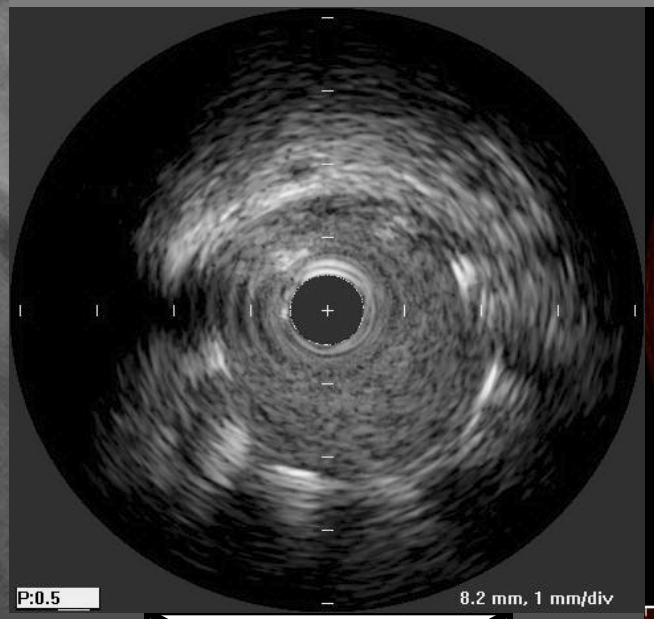


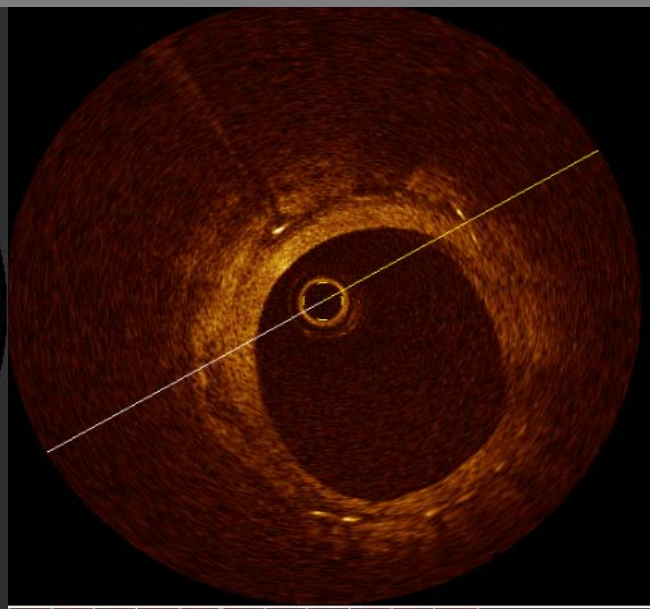


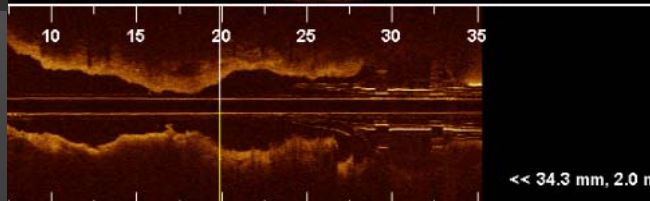












BIOLIMUS-STEALTH

randomization

DES with Bioabsorbable Polymers

- BioMatrix (Biosensors)
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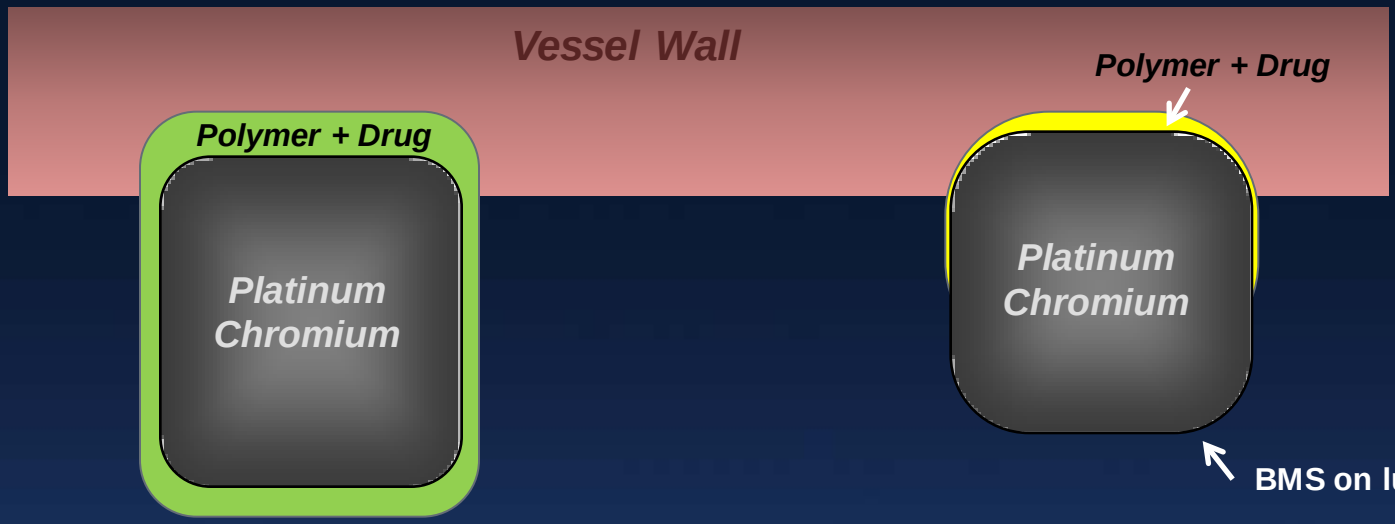
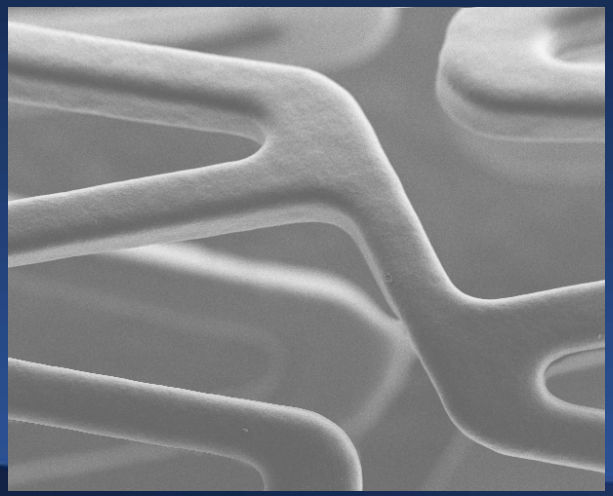
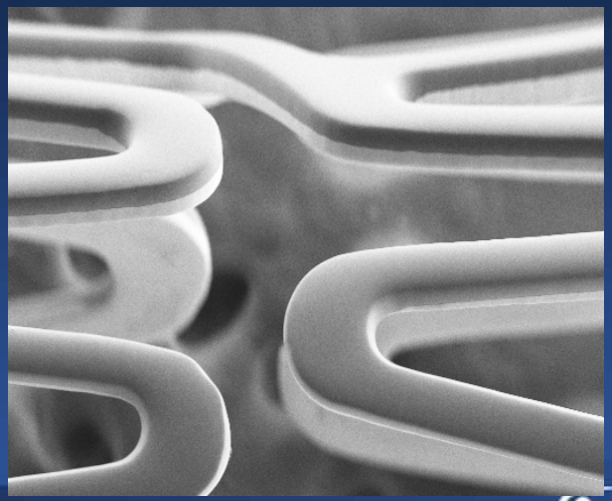
Drug-Eluting Technology Progression

Current DES
Conformal Biostable Polymer

SYNERGY™ DES
Abluminal Bioabsorbable Polymer







EVOLVE Study Design

Patients with de novo native coronary lesions
≤28 mm in length, RVD ≥2.25 mm ≤ 3.5, %DS >50
(excluded LM disease, CTO, AMI or recent MI)

Randomized 1:1:1 at 29 sites
(EU, Australia, New Zealand)

PROMUS Element	SYNERGY	SYNERGY ½ Dose
N=98	N=94	N=99

Single-blind, noninferiority design

Primary Clinical Endpoint: TLF (TV-CD, TV-MI, or TLR) at 30 days

Primary Angiographic Endpoint: In-stent late loss at 6 months

EVOLVE FHU (SYNERGY™ Stent)

Angiographic Outcomes at 6 Months

In-stent values	PROMUS Element™ N=98	SYNERGY N=94	*P* value	SYNERGY ½ Dose N=99	*P* value
MLD	2.29 ± 0.50	2.41 ± 0.42	0.08	2.45 ± 0.44	0.02
Late Loss	0.15 ± 0.34	0.10 ± 0.25	0.19	0.13 ± 0.26	0.56
Diameter stenosis	8.95 ± 14.97	6.59 ± 9.90	0.18	7.27 ± 9.47	0.34
Binary restenosis	3.2%	0.0%	0.25	0.0%	0.25

Assessed by QCA
Values are mm or percent
Intent-to-treat; *P* values are versus PROMUS Element

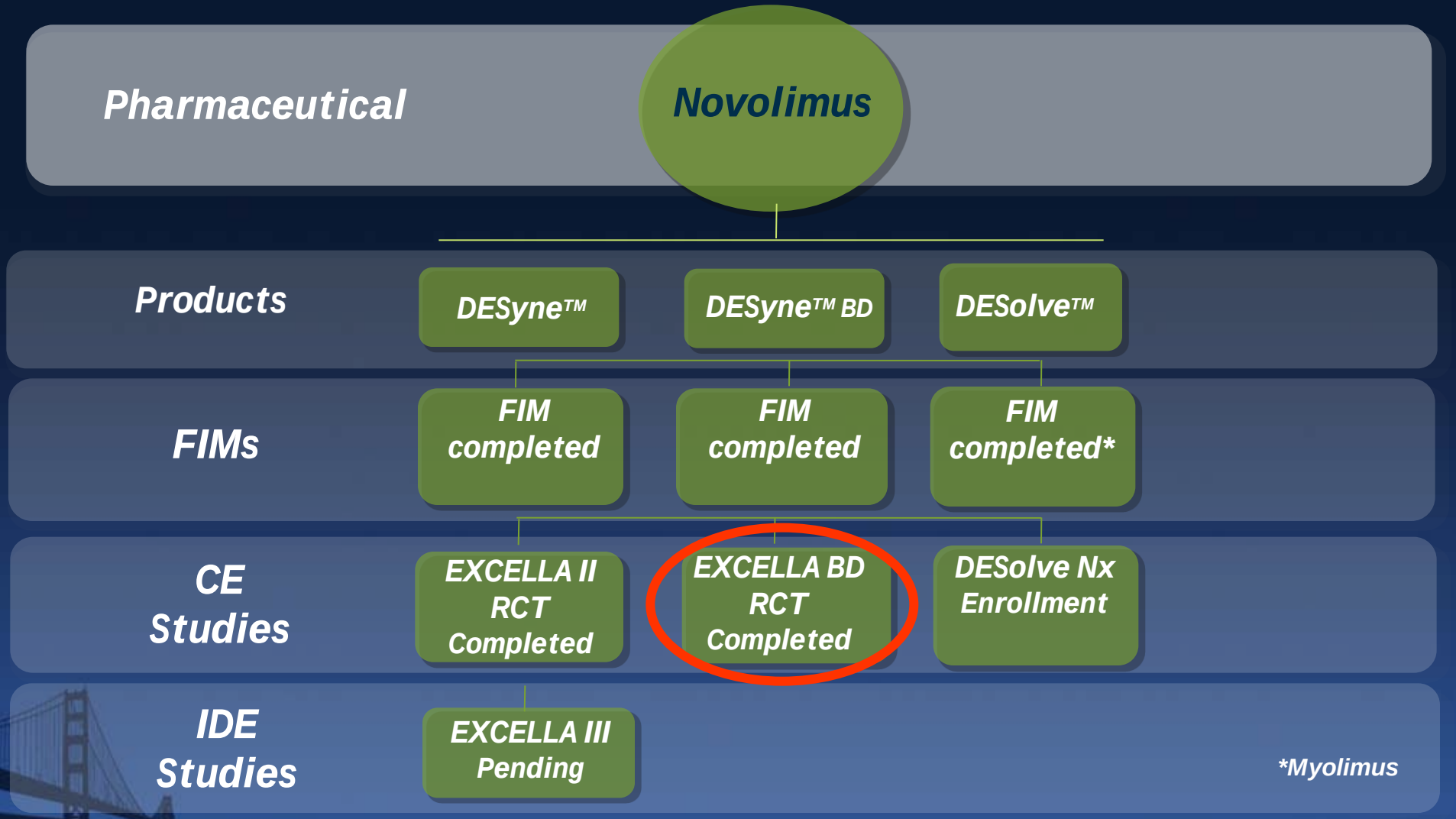
Presented by Ian Meredith, MBBS, PhD at TCT 2011. The SYNERGY™ Stent is an investigational device and not for sale. This material is not intended for use in the US and Japan.

See Glossary

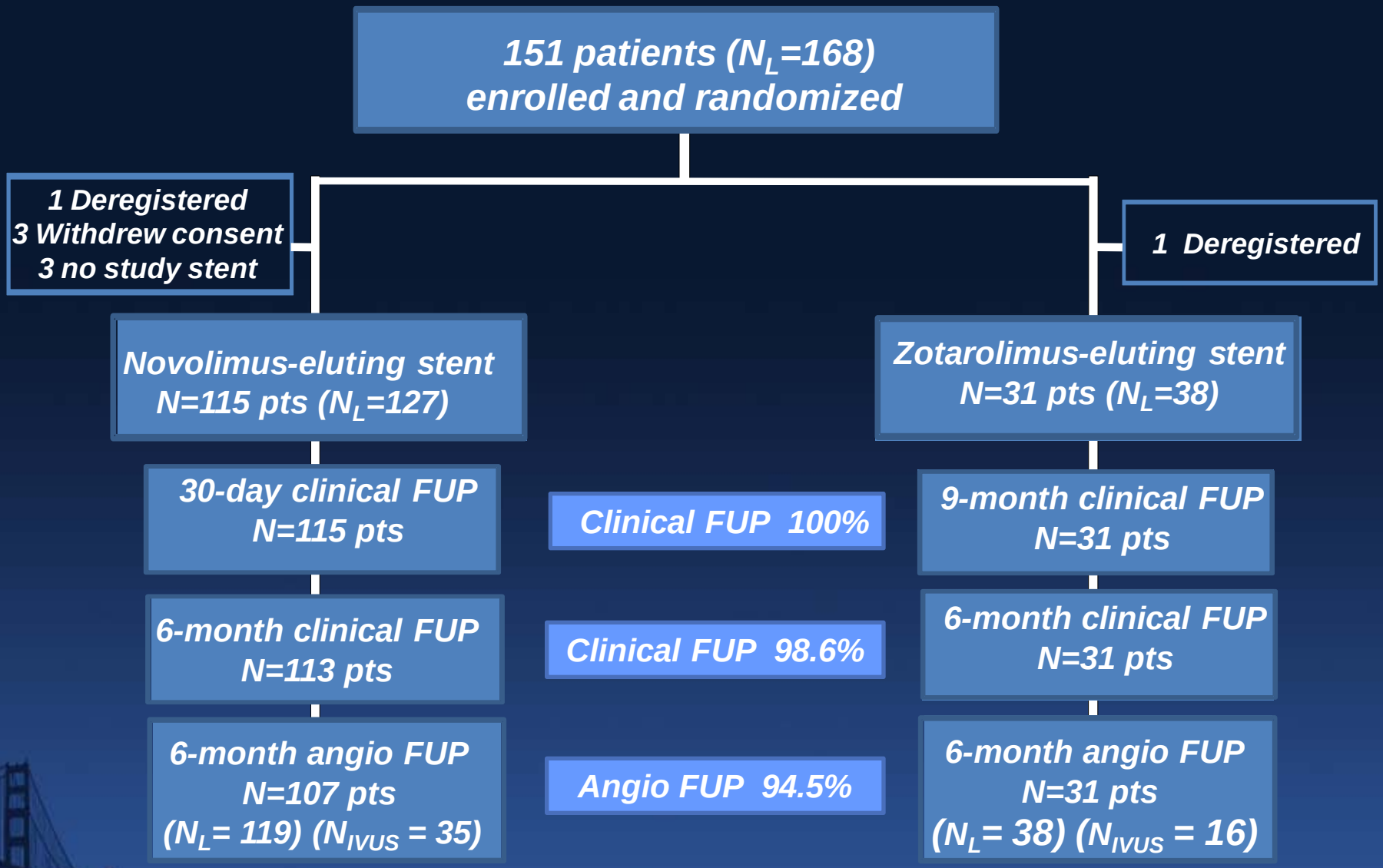
Bioabsorbable Polymer DES Systems

- BioMatrix (Biosensors)
- Synergy (Boston Scientific)
- DESyne (Elixir)
- Inspiron (Scitech)
- Sirolimus + EPC capture (Orbus)
- Biomine (Merril Life Science)

Elixir clinical programs running in parallel across three platforms



Patient Flow and Follow-up



Intention to treat analysis

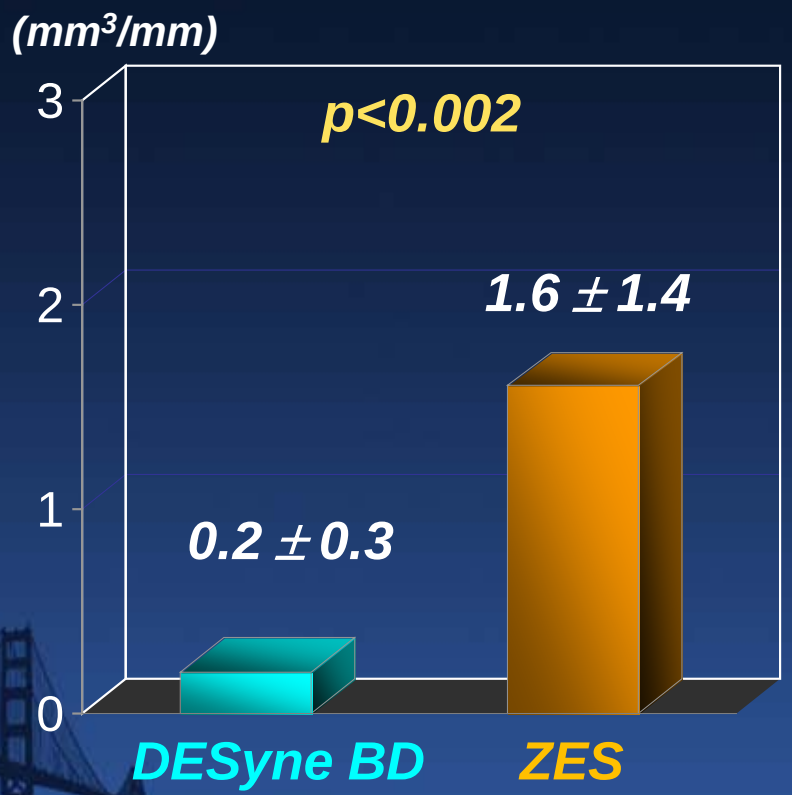
Pts, patients; N_L number of lesions; N_{IVUS} number of IVUS

Angiographic Results 6 months

In-Stent Analysis	Novolimus	Zotarolimus	P value
RVD. mm	$N_{(L)}$=119	$N_{(L)}$= 38	
Post-procedure	3.00±0.37	3.08±0.35	0.31
At 6-months	2.95±0.37	2.99±0.38	0.67
MLD / Late Lumen loss (LLL), (mm)			
Acute gain	1.87±0.42	2.01±0.43	0.09
MLD post-procedure	2.76±0.37	2.90±0.34	0.04
MLD at 6-months	2.64±0.39	2.22±0.53	<0.001
LLL at 6-months (in-stent)	**0.12±0.15**	**0.67±0.47**	**< 0.001**
Diameter Stenosis (%)			
Post-procedure	8.5±44	6.2±4.5	0.002
At 6-months	11.0±6.6	25.6±15.1	< 0.001
Binary Restenosis (%) (in-stent)	0.0%	7.9%	0.003

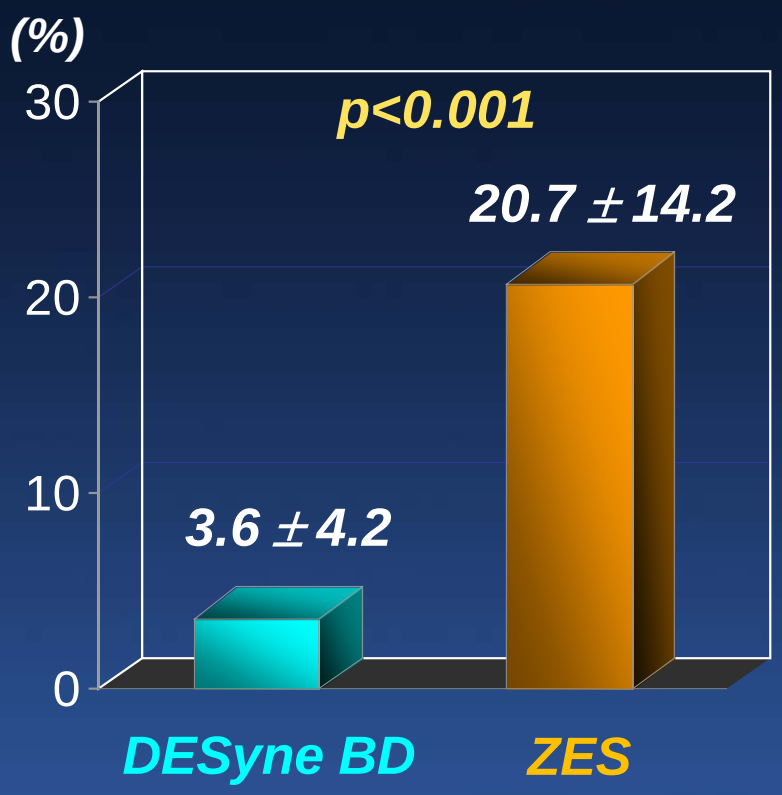
DESyne BD 6-month Follow-up IVUS

Neointimal Volume Index



% Neointimal Volume

(NIH volume/Stent volume)



Follow-up 3D IVUS analysis: DESyne =35 ZES =16

DES with Bioabsorbable Polymers

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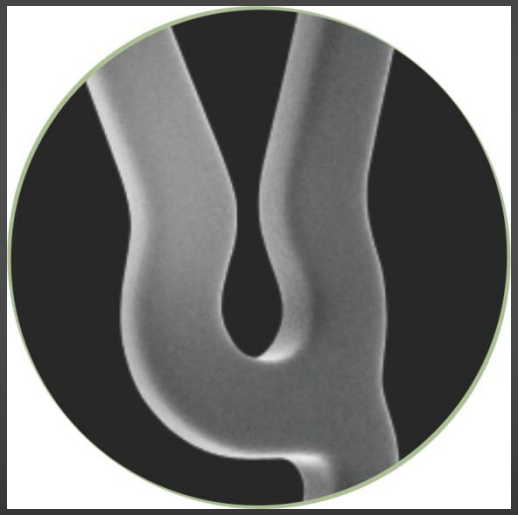
INSPIRON Sirolimus-Eluting Stent

Plataforma
CoCr – L605

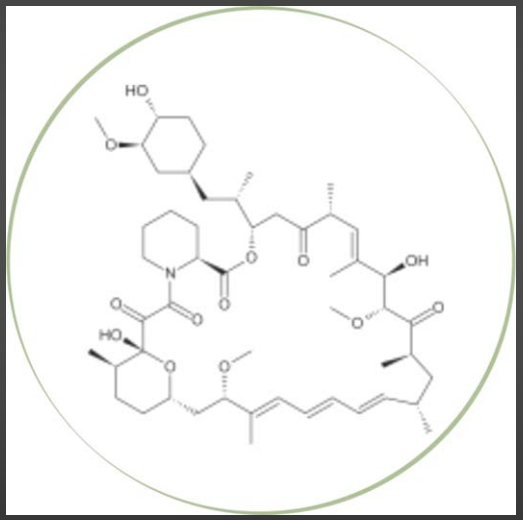
80 µm

Polímero
Biodegradável



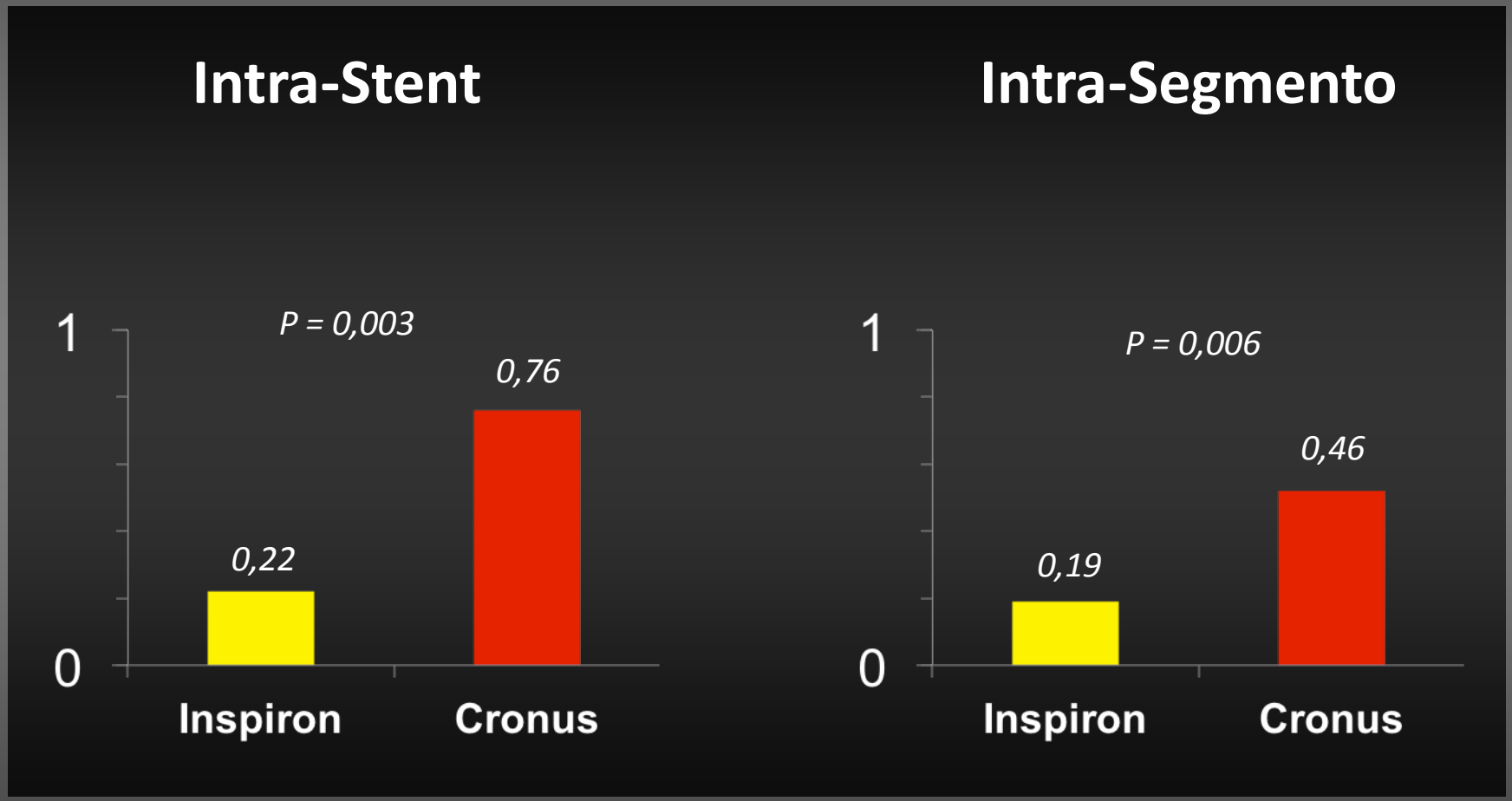
PLA + PLGA

Droga
Sirolimus



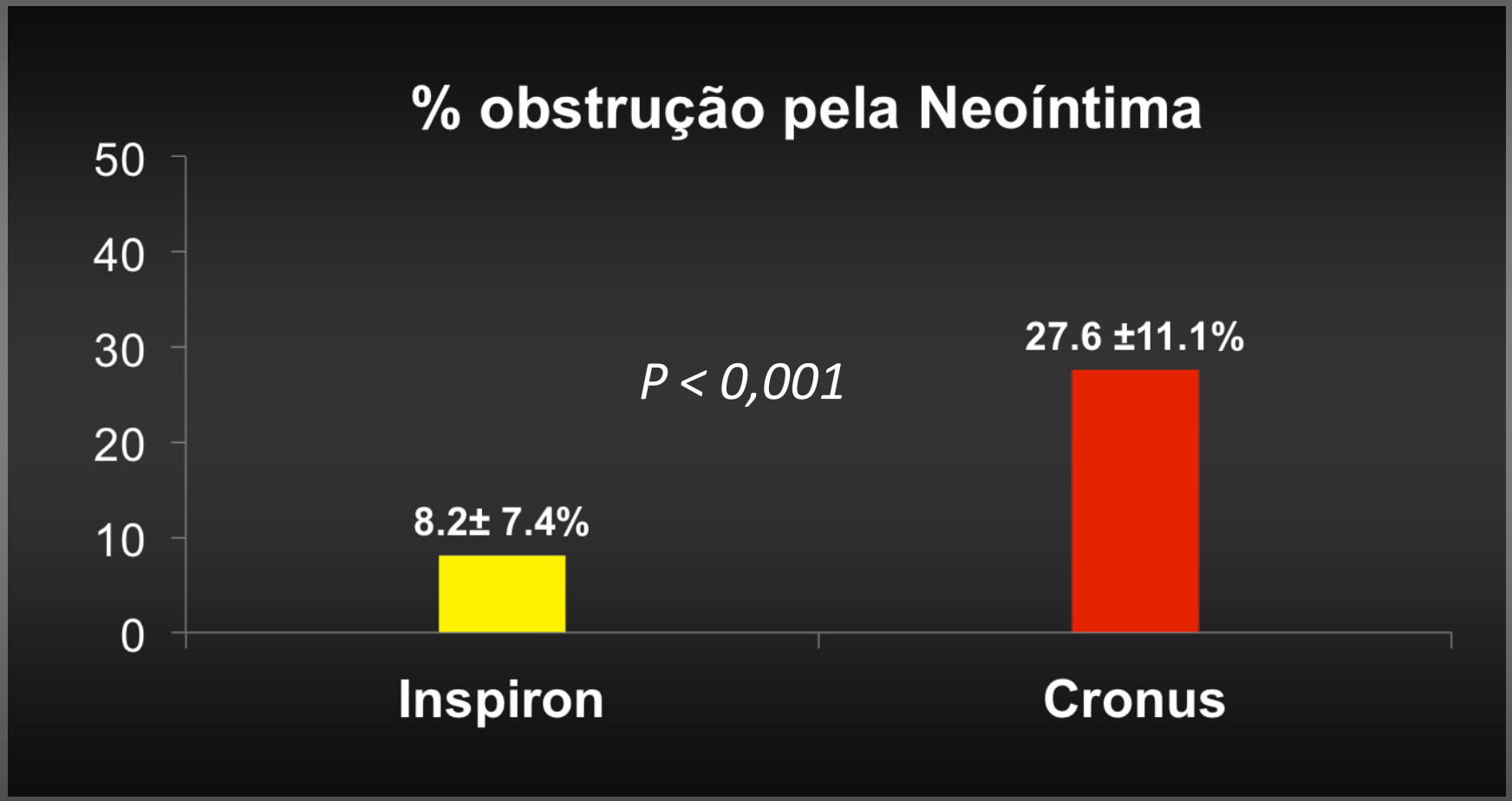
1,4 µg/mm^2

Perda Luminal Tardia aos 6 meses



Lemos, Ribeiro, Perin, et al

USIC aos 6 meses



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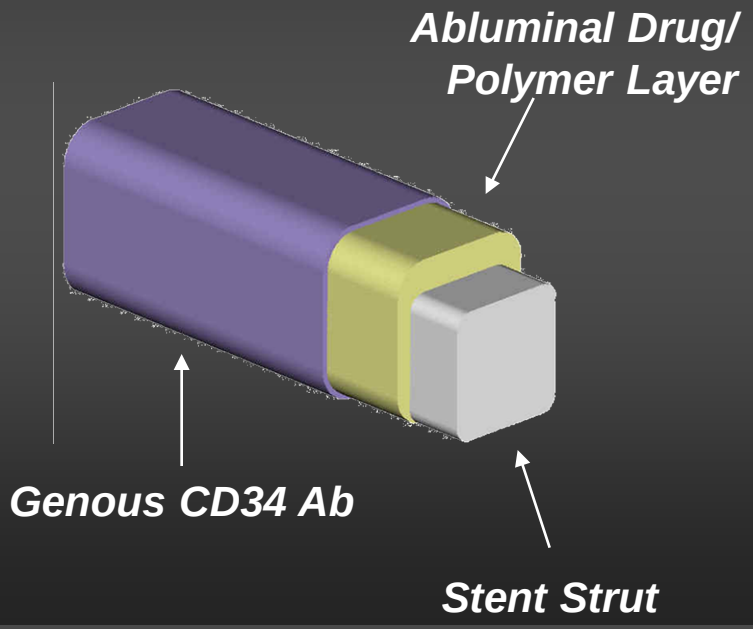
Directional Sirolimus Biodegradable Abluminal Coating and Anti-CD34 Surface Modification: Device Description

Genous Technology:

- Anti-CD34 surface to promote healing through rapid stent endothelialization.

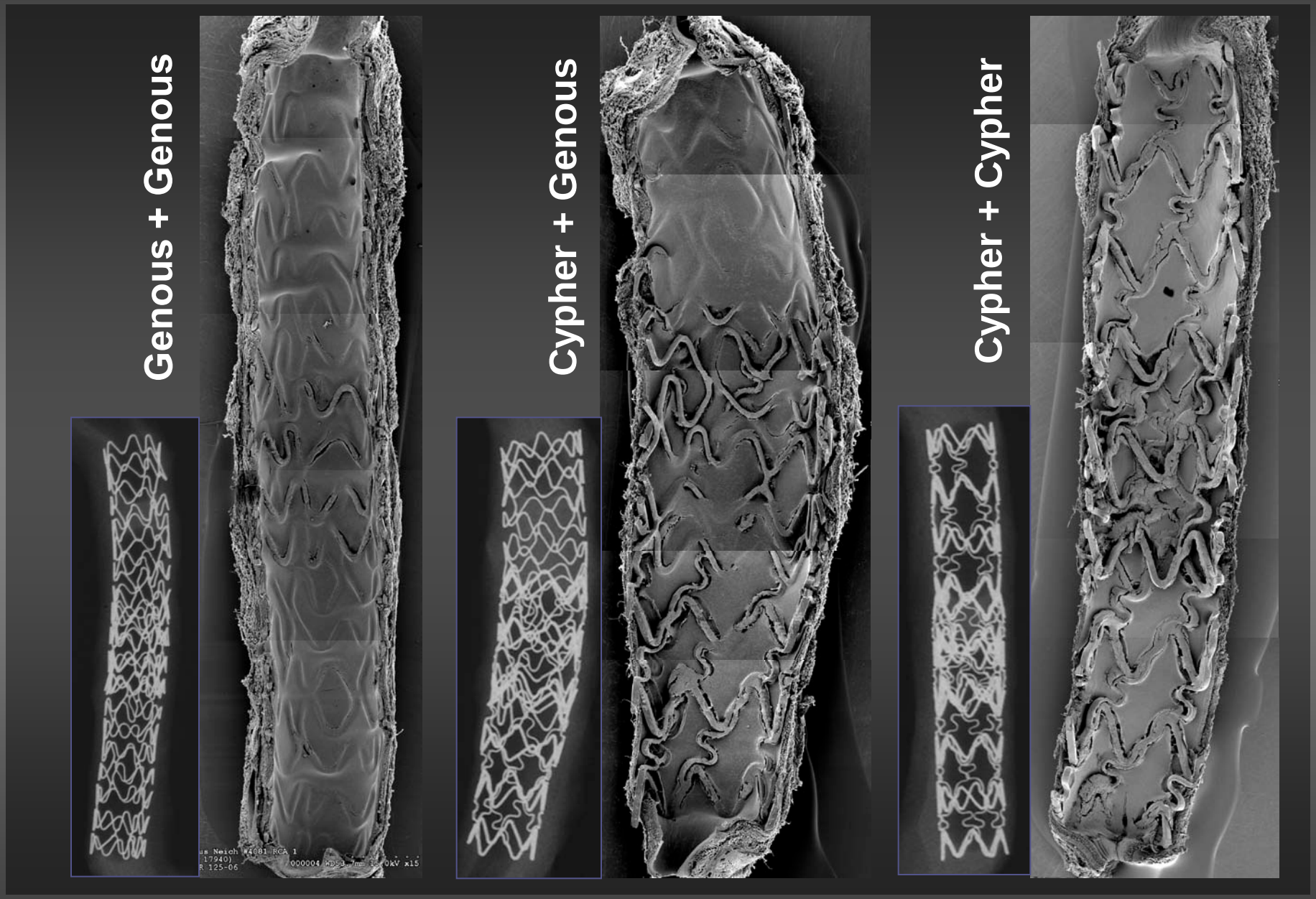
Genous-DES Technology:

- Rapamycin (5 µg/mm) applied in biodegradable SynBiosys polymer on the abluminal side.



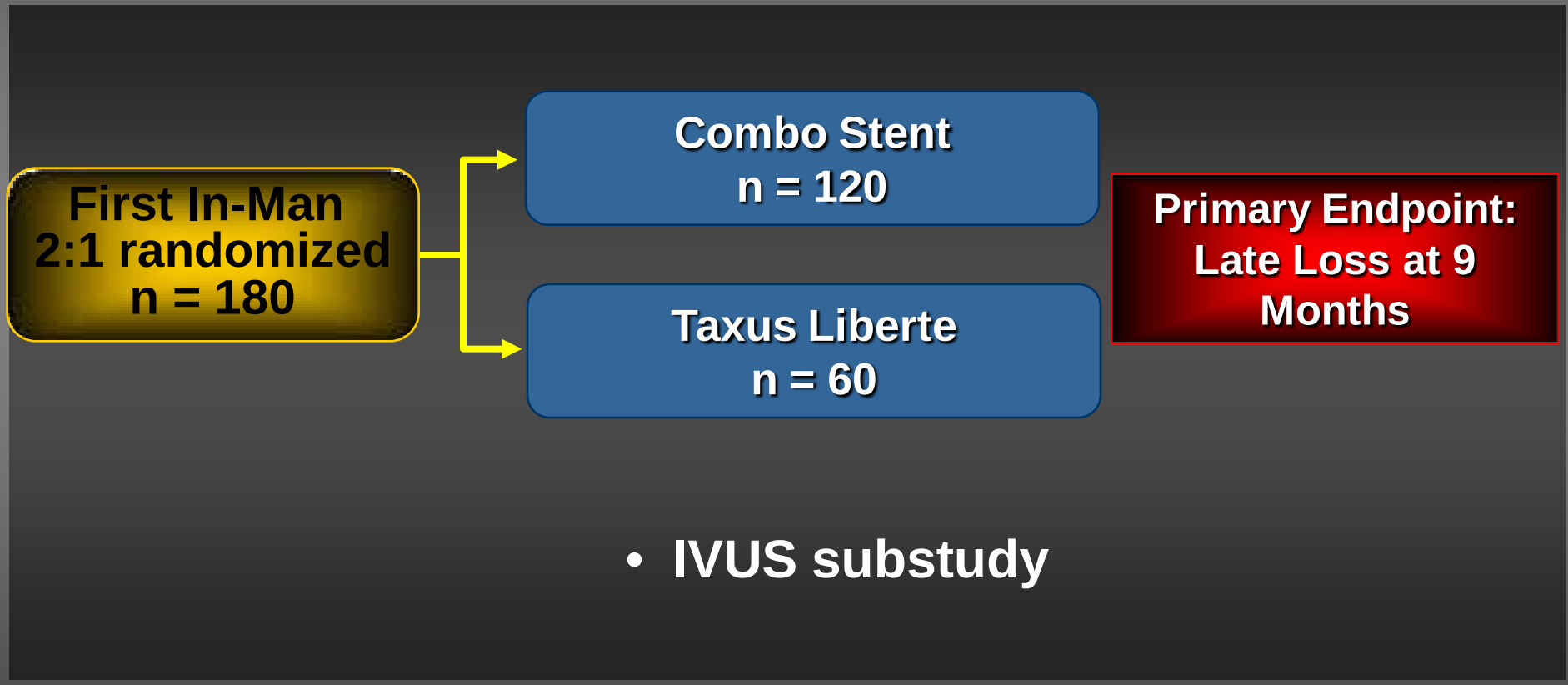
Juan Granada et al.

14-Day Porcine Coronary Artery SEM - Overlapping



REMEDEE (Sirolimus + EPC)

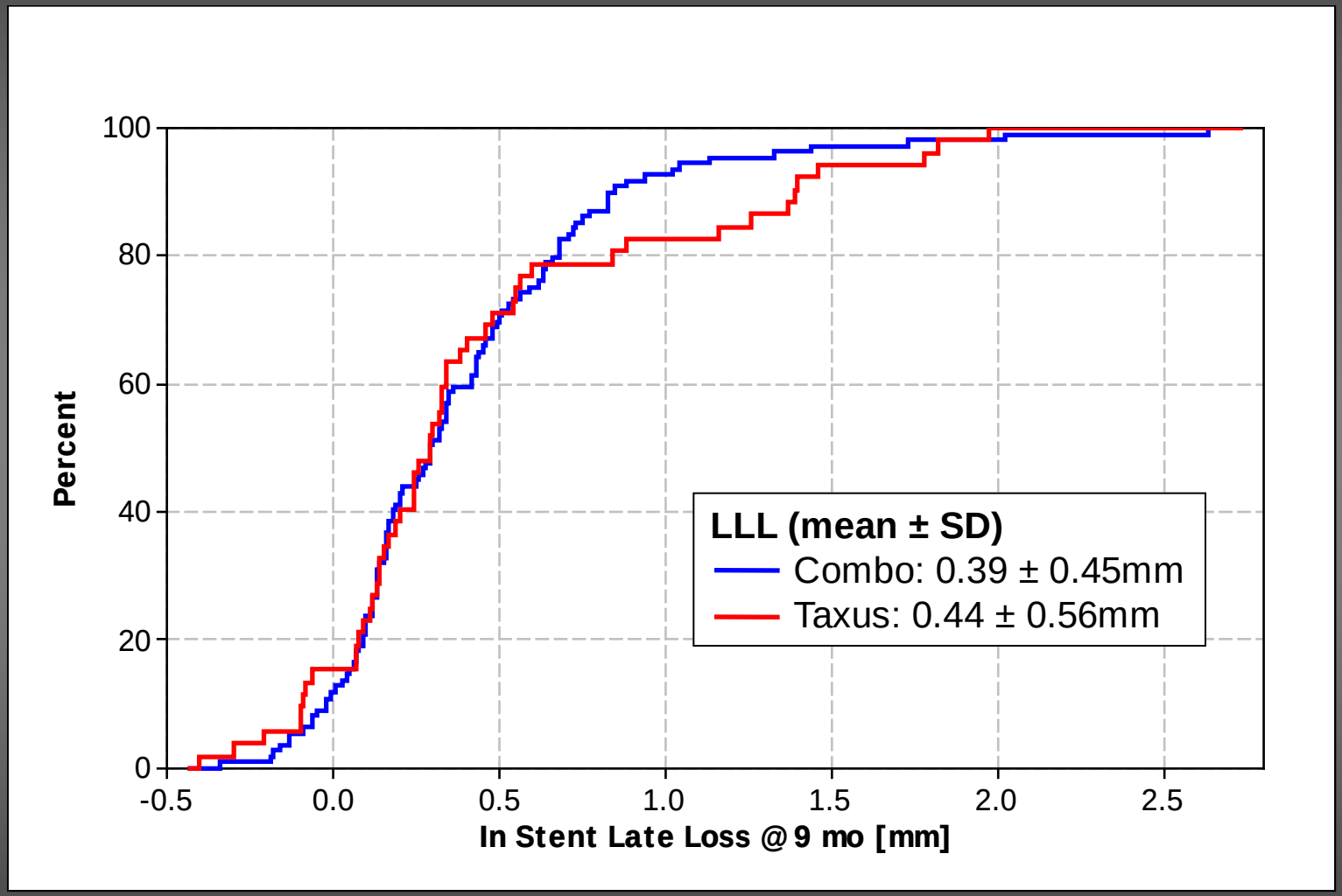
Randomized Evaluation of an abluMinal sirolimus coatED bio-Engineered stEnt



- IVUS substudy

In-stent Late Lumen Loss at 9 Months

Cumulative Frequency Distribution



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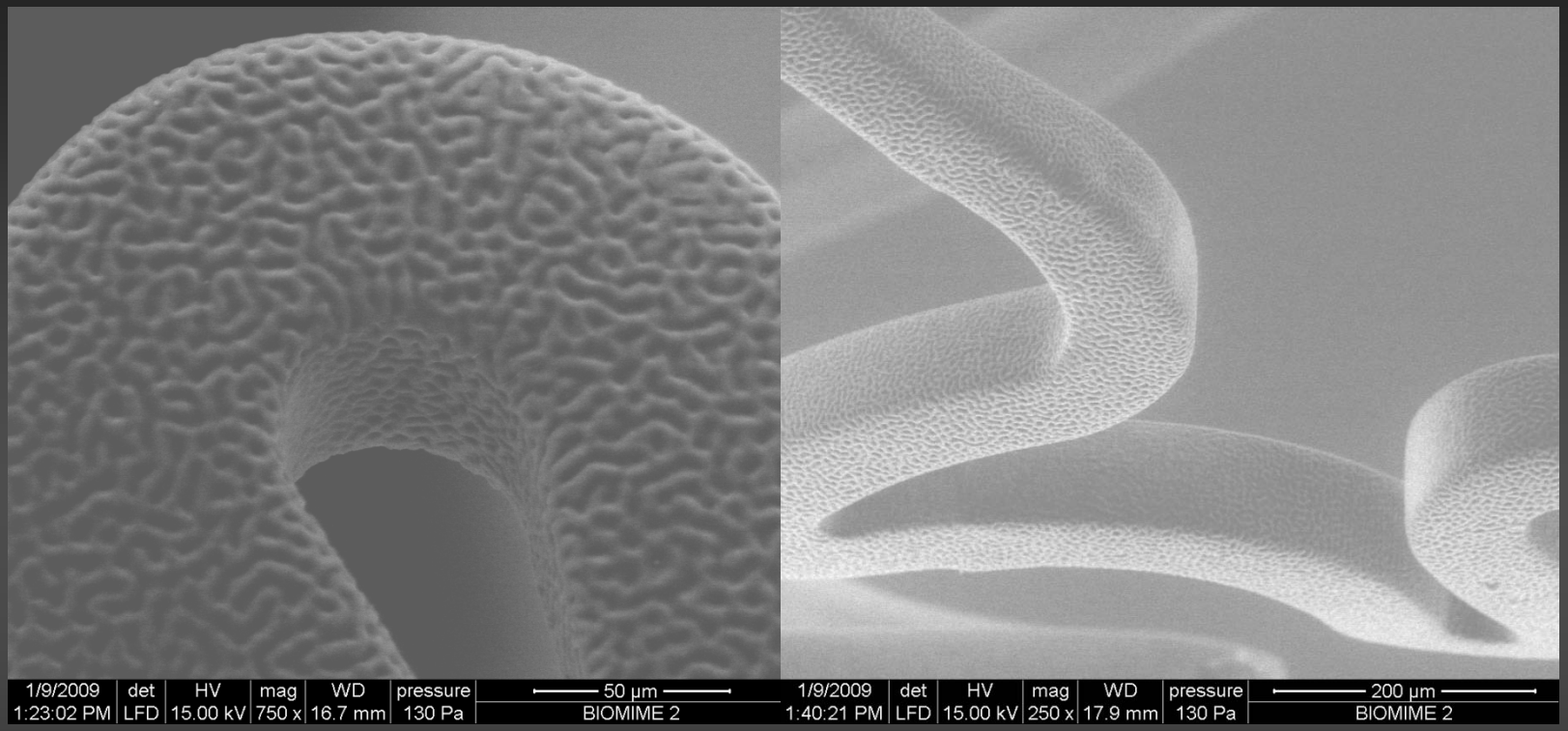
BioMime Coating Integrity



After inflation **After inflation**

It is important to know that post inflation. BioPoly™ adjusts to stresses generated at vulnerable areas – s-links & y-connectors due to its high elasticity

Data on file. SEM picutures BioMime Stent

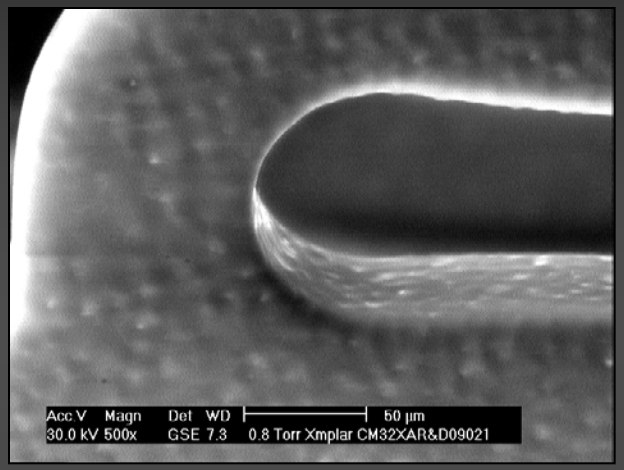
Merit 2: QCA at 8 months
132 lesion / 97 patients

- **Late Loss**
  - In-segment 0.13 [0.09, 0.31]
  - In-stent 0.15 [0.09, 0.33]
- **Restenoses**
  - In-segment 6 / 132 (4.5%)
  - In-stent 1/ 132 (0.8%)

Cortesia de Ricardo Costa

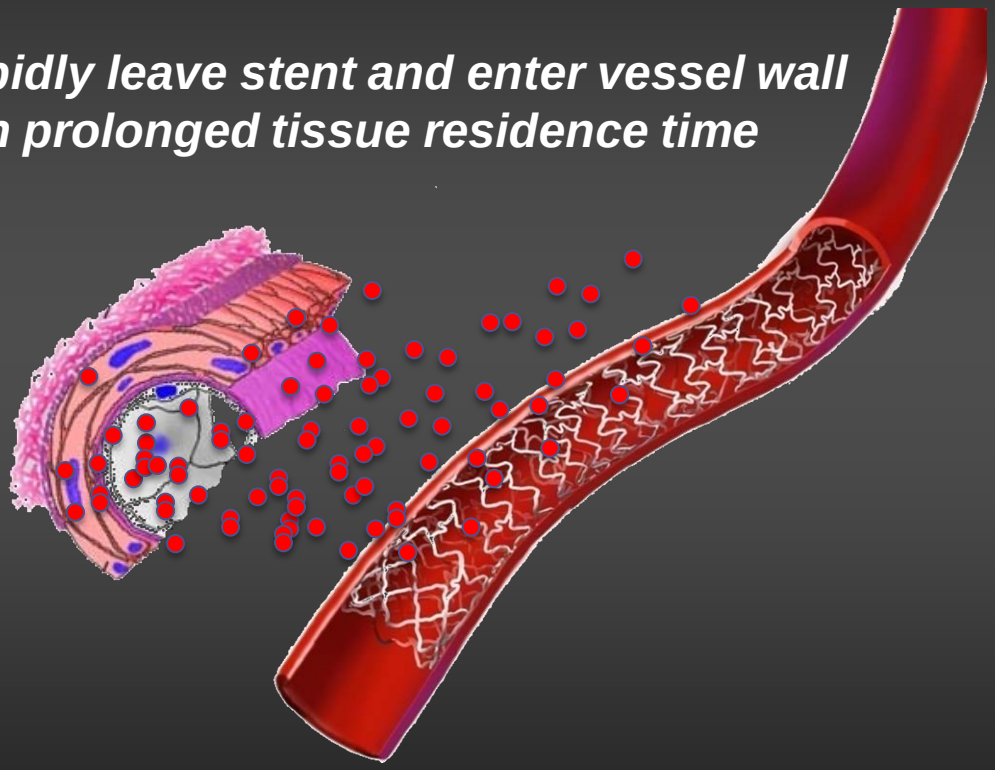
Nanotechnology – Polymer Free

Unique Formulation - Solid lipid nano-spheres (SLN) consisting of Merilimus + Lipid (<300 nm)



SEM Image of Stent struts coated with nano-formulation

SLN rapidly leave stent and enter vessel wall with prolonged tissue residence time



Average particle size 165nm. High nano particle stability

DES Evolution

Durable Polymers

Bioabsorbable Polymers

Non-polymeric

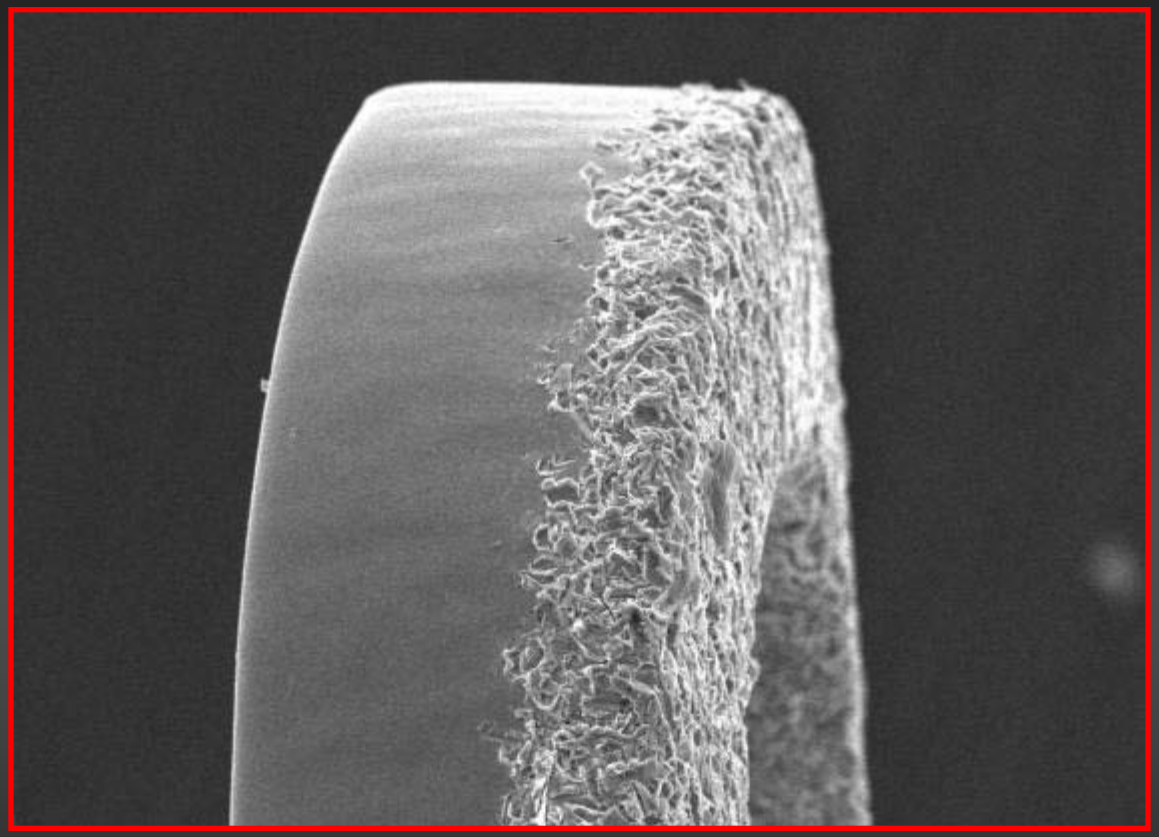
Bioabsorbable Scaffold

Non-Polymeric DES

- BioFreedom (Biosensors)
- Translumina (Translumina)
- Vestasync (MIV)
- Cre8 (CID)
- Medtronic prototype

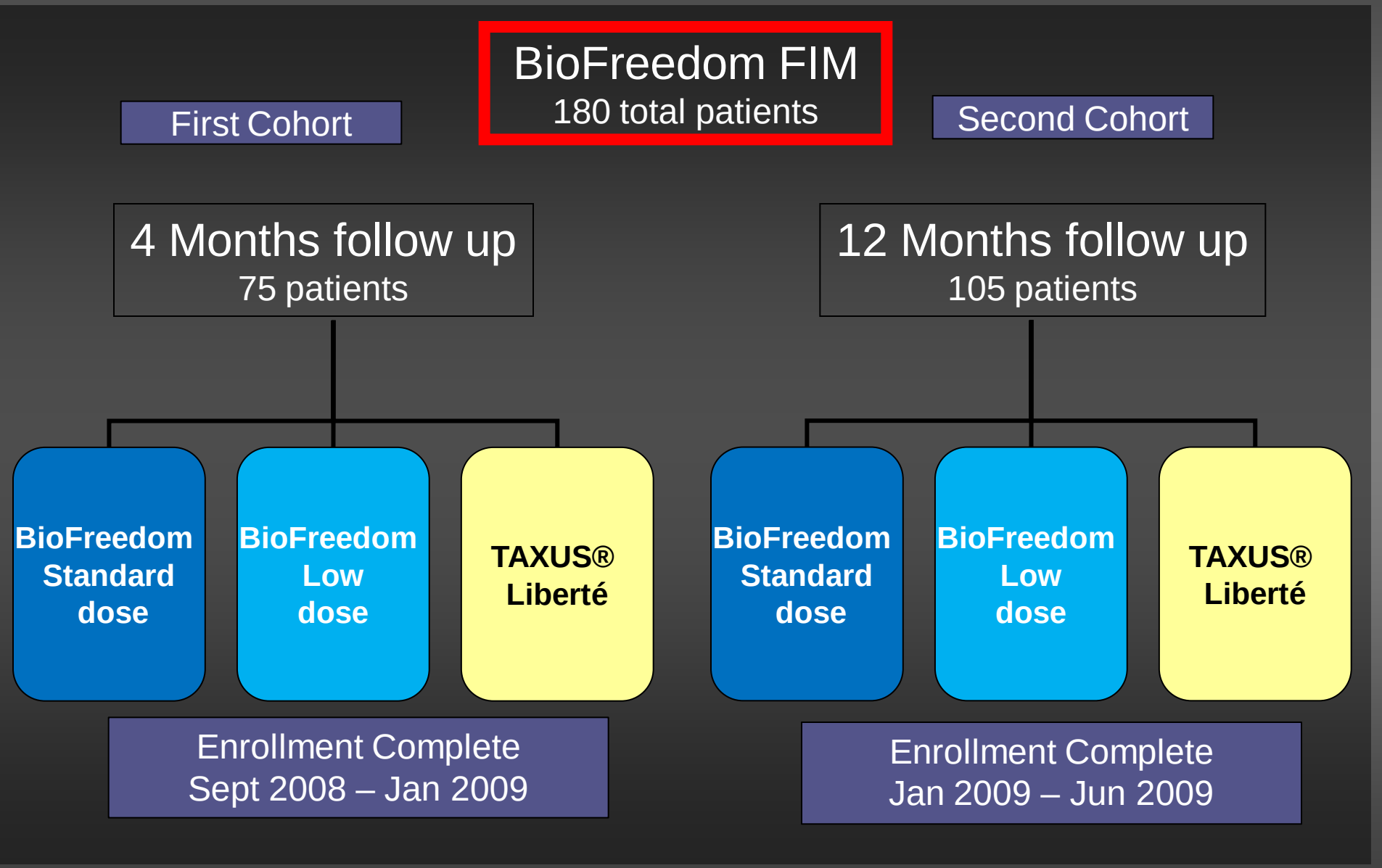
BioMatrix Freedom Stent

Micro-structured Surface



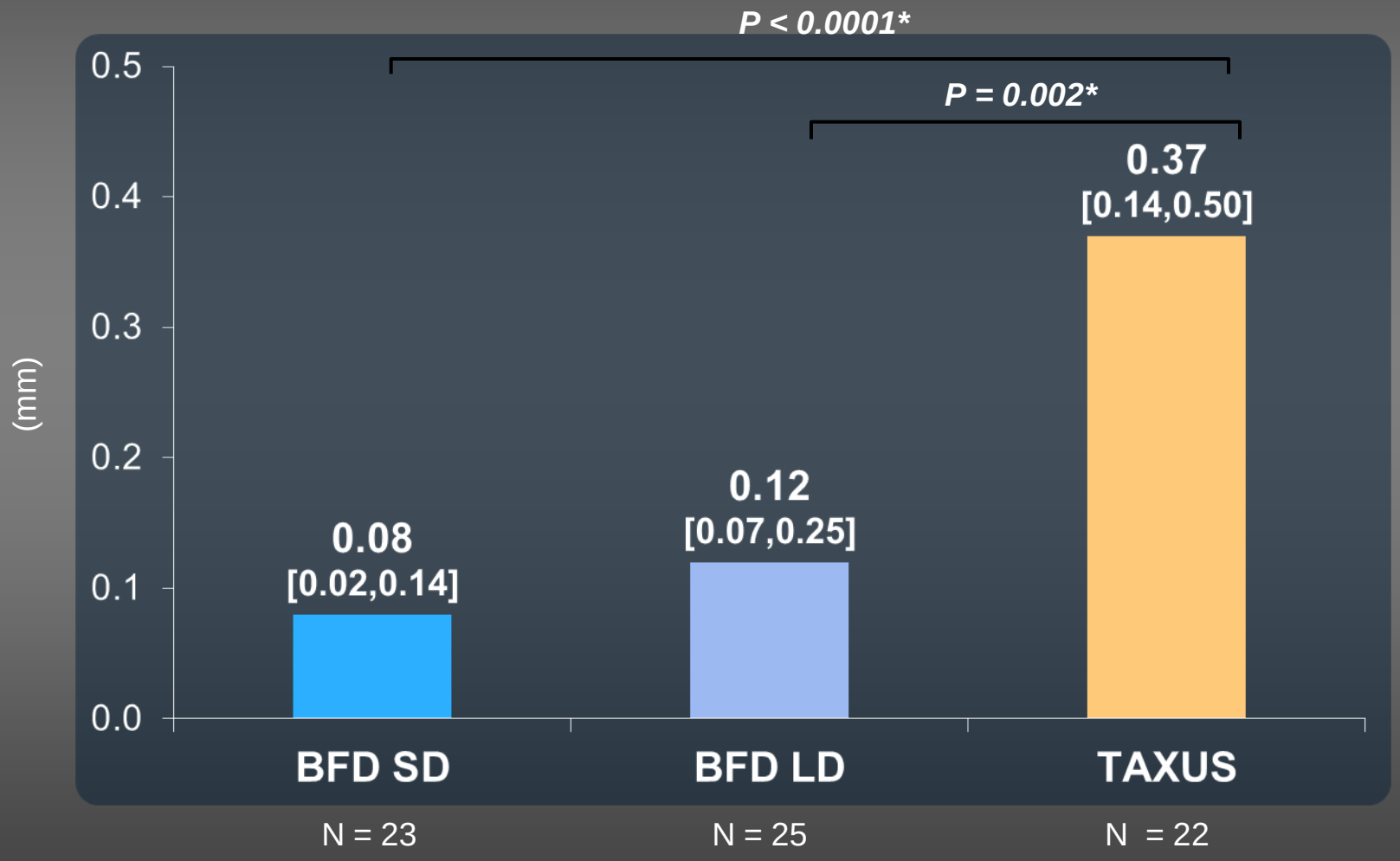
- Selectively micro-structured surface holds drug in abluminal surface structures

BioFreedom FIM Design



In-Stent LLL at 4 Months FU

1st Cohort – SECONDARY ENDPOINT

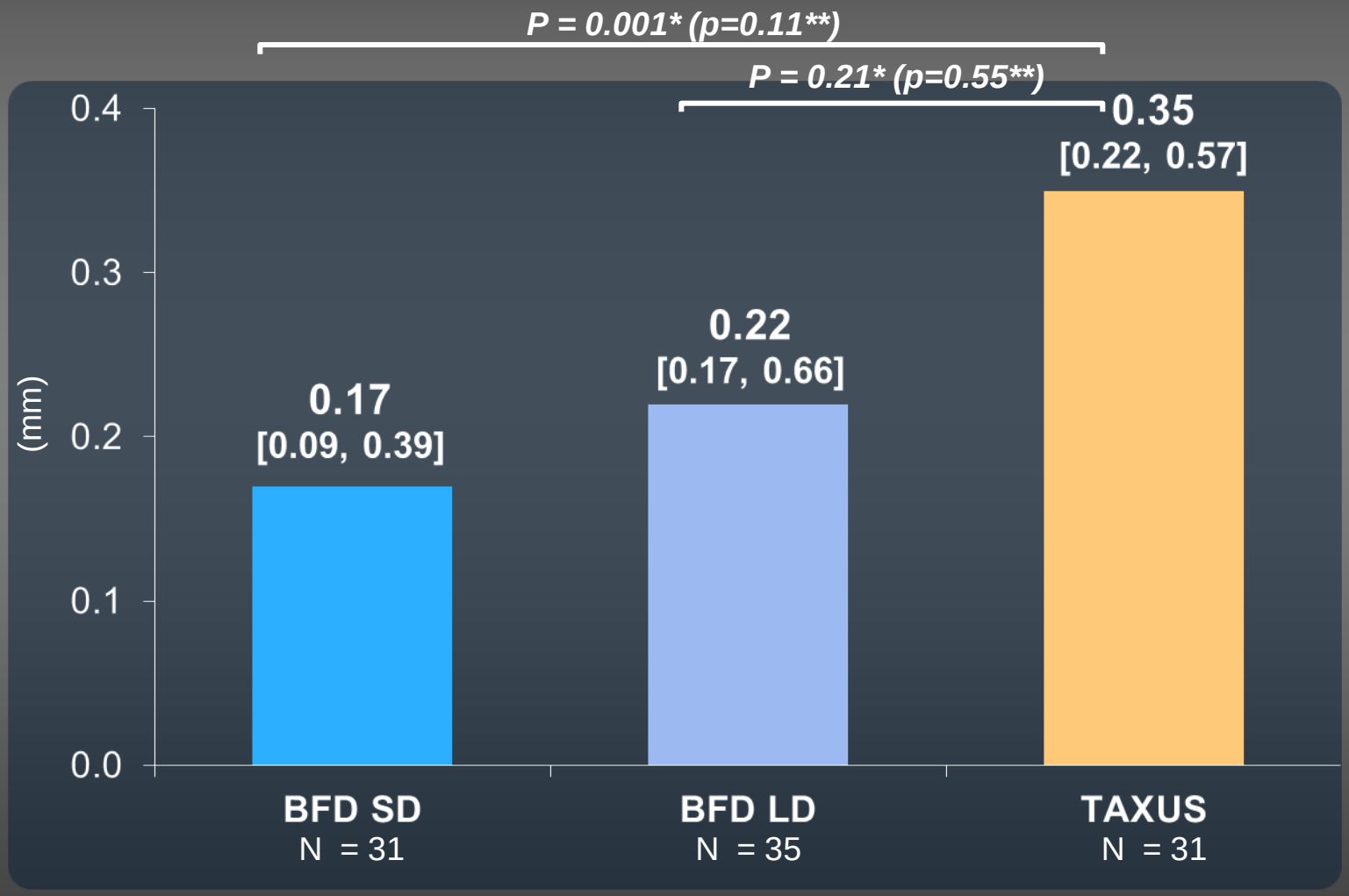


*Superiority tests.

Grube E., oral presentation, TCT 2010

In-Stent LLL at 12 Months FU

2nd Cohort – PRIMARY ENDPOINT

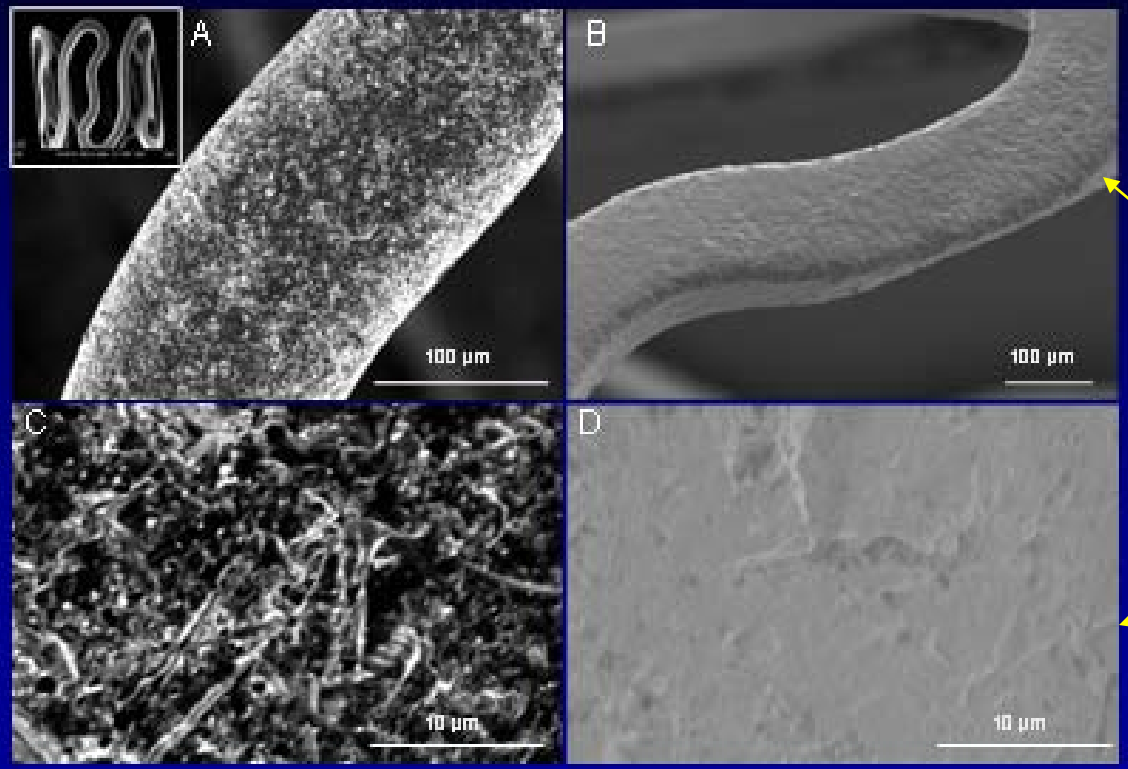


*Non-inferiority tests. **Superiority tests.

Grube E., oral presentation, TCT 2010

Translumina Porous Surface Stent

Unique microporous stent surface



before coating after

Pure Sirolimus

ISAR-TEST 2:
Testing Dual-Drug Sirolimus + Probucol

1007 pts with de-novo lesions randomized

Cypher	Dual DES	Endeavor
(n=333)	(n=335)	(n=339)

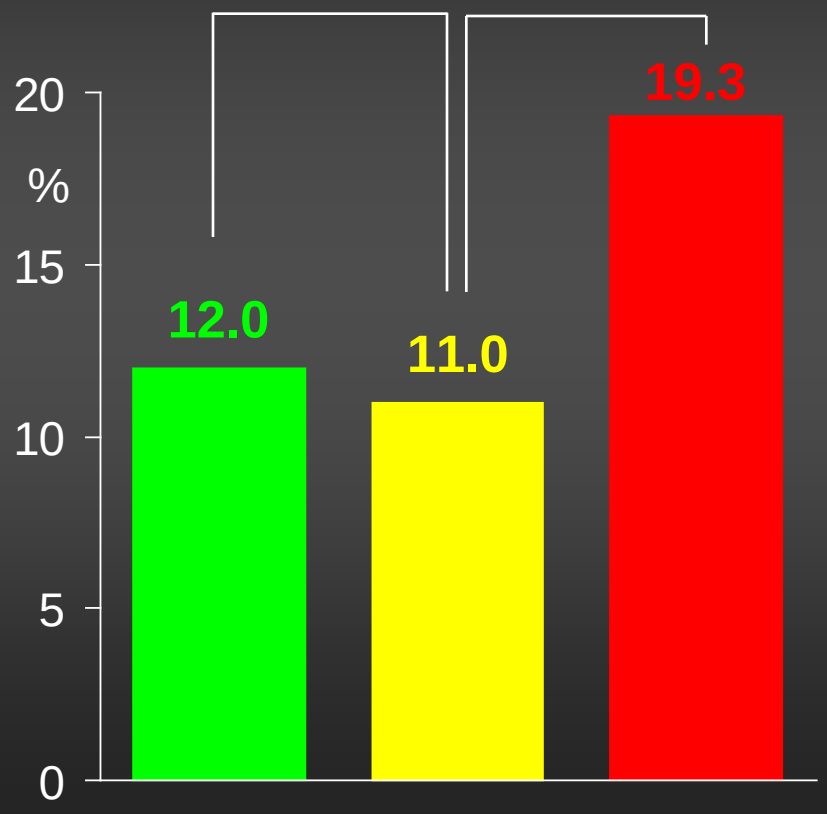
Polymer-free,
probucol + sirolimus-eluting stent

Primary Endpoint: angiographic restenosis
Secondary Endpoint: TLR

R Byrne et al., *Eur Heart J* 2009

ISAR-TEST-2: Restenosis Analysis

Angiographic Restenosis (1^{ary} EP)

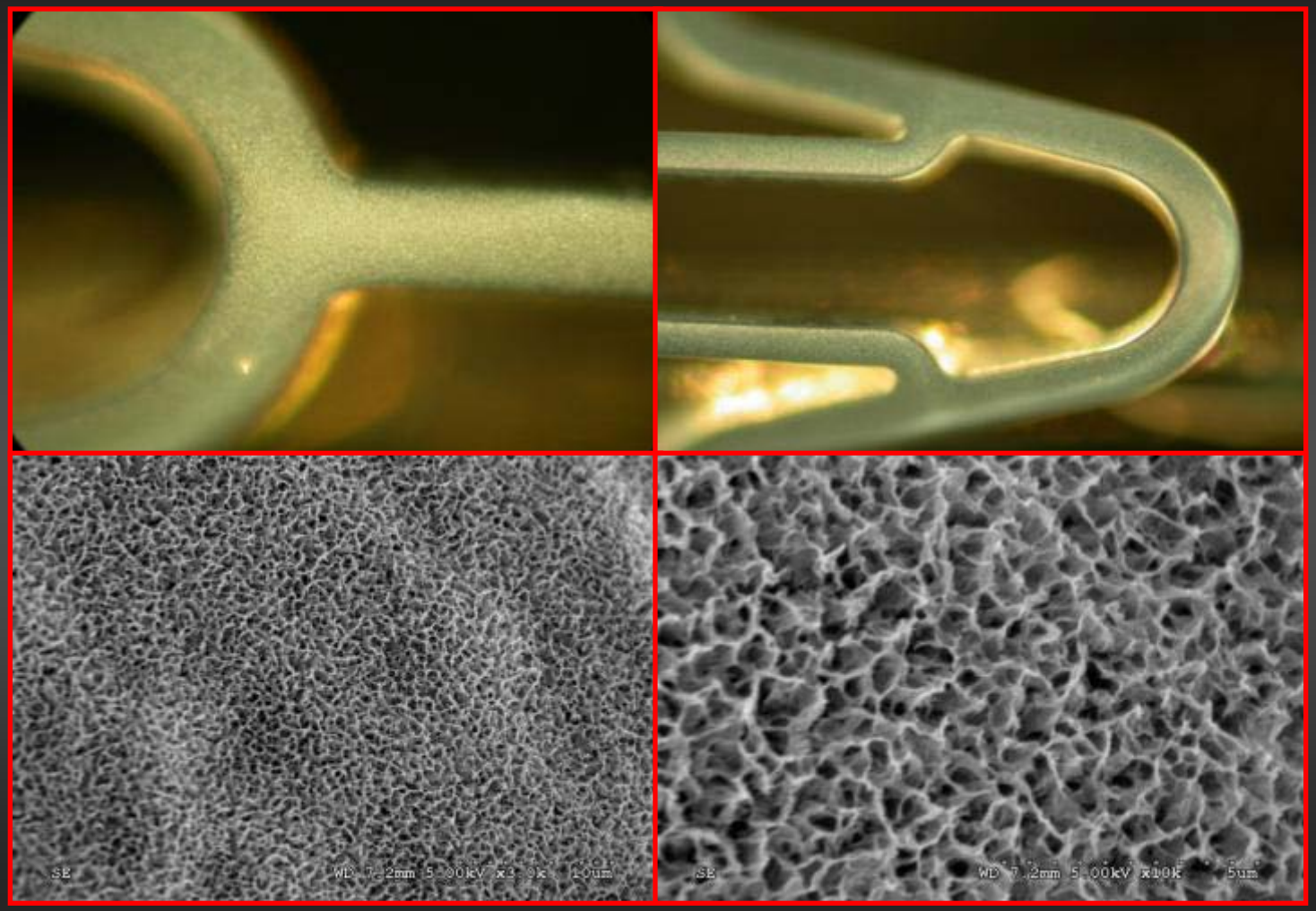


Clinical Restenosis (TLR)

Cypher Dual-DES Endeavor

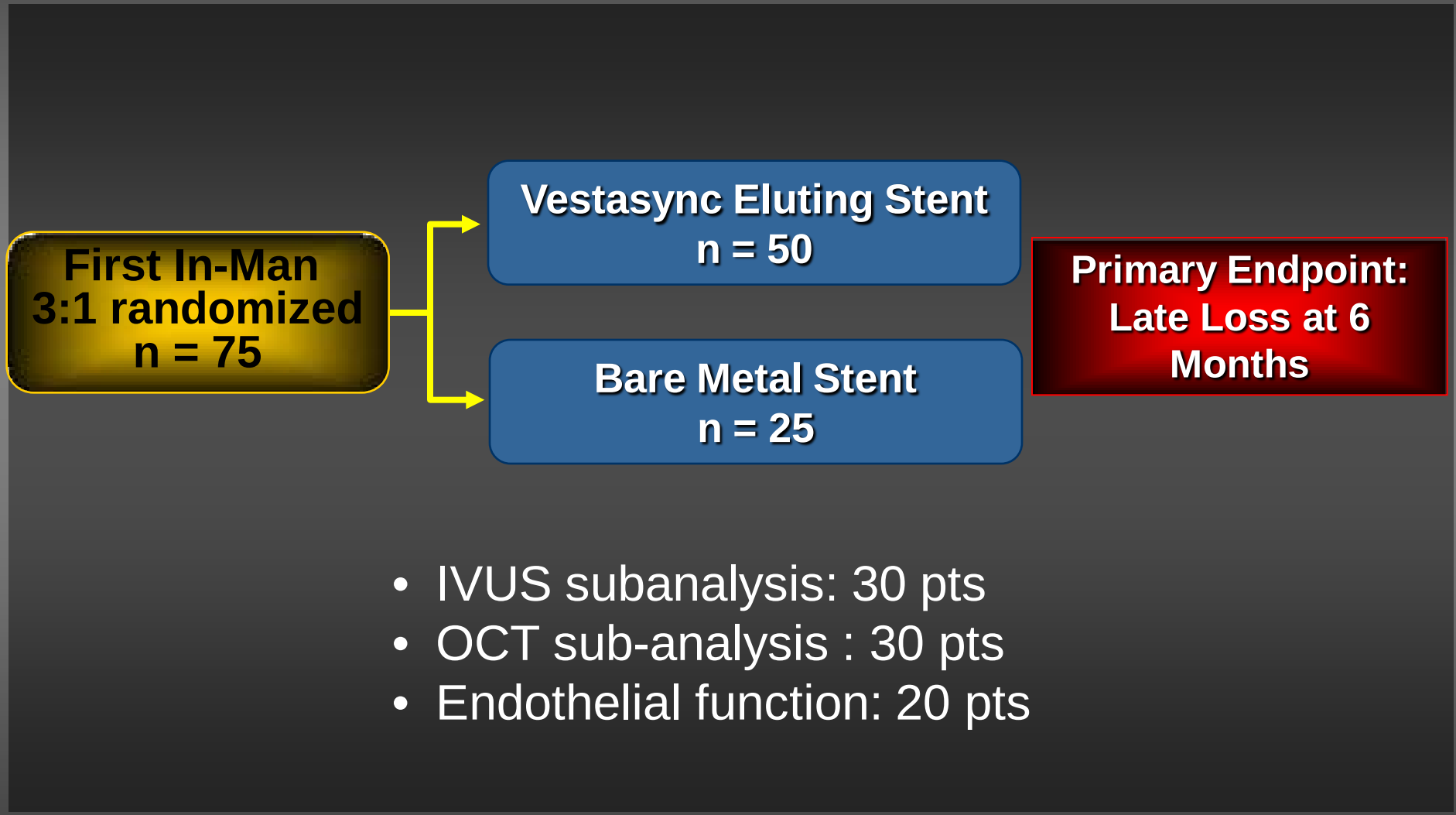
R Byrne et al., *Eur Heart J* 2009

3D MicroPorous Nanofilm HAp



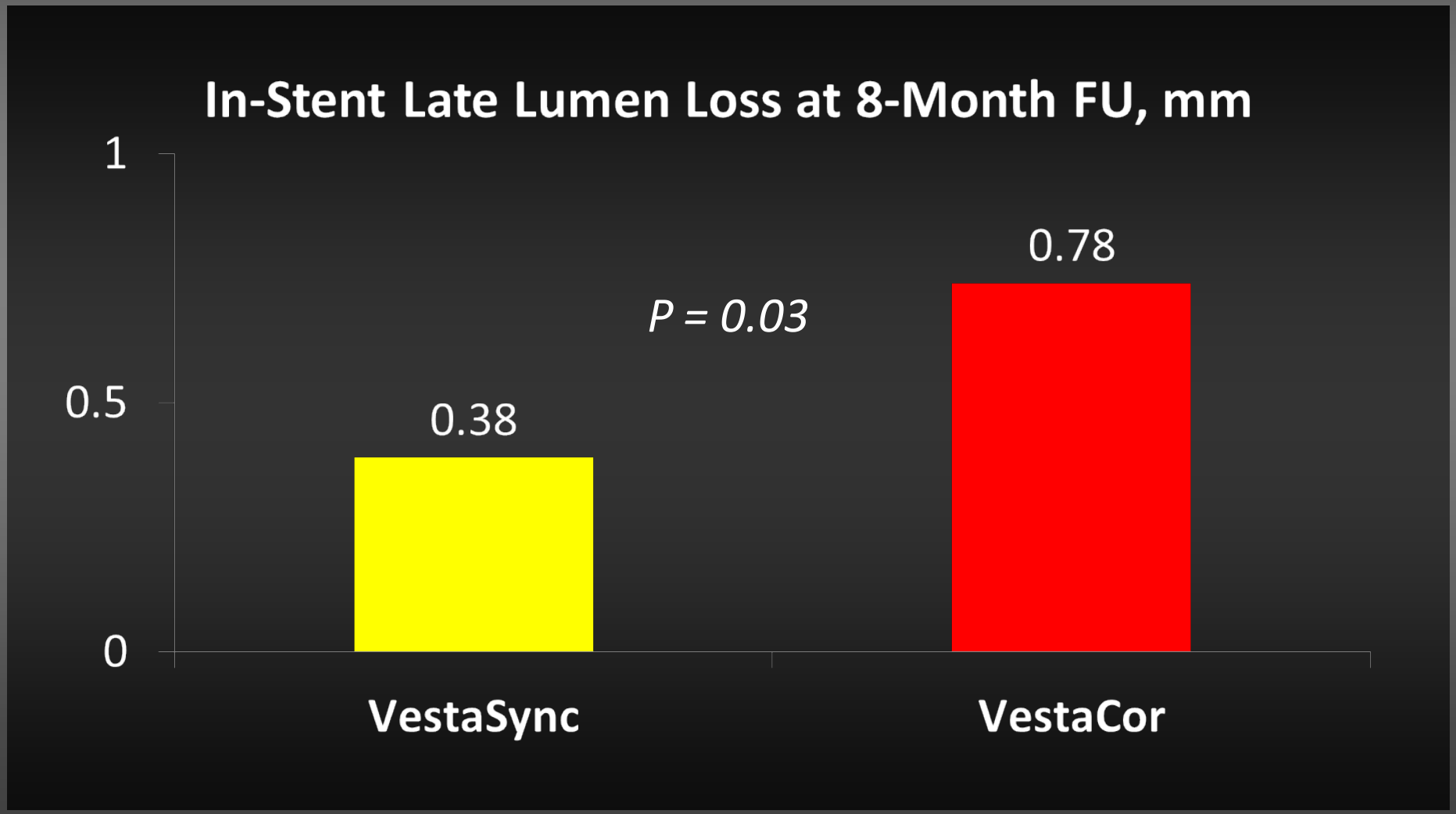
VESTASYNC II

Polymer-Free Sirolimus-Eluting Stent

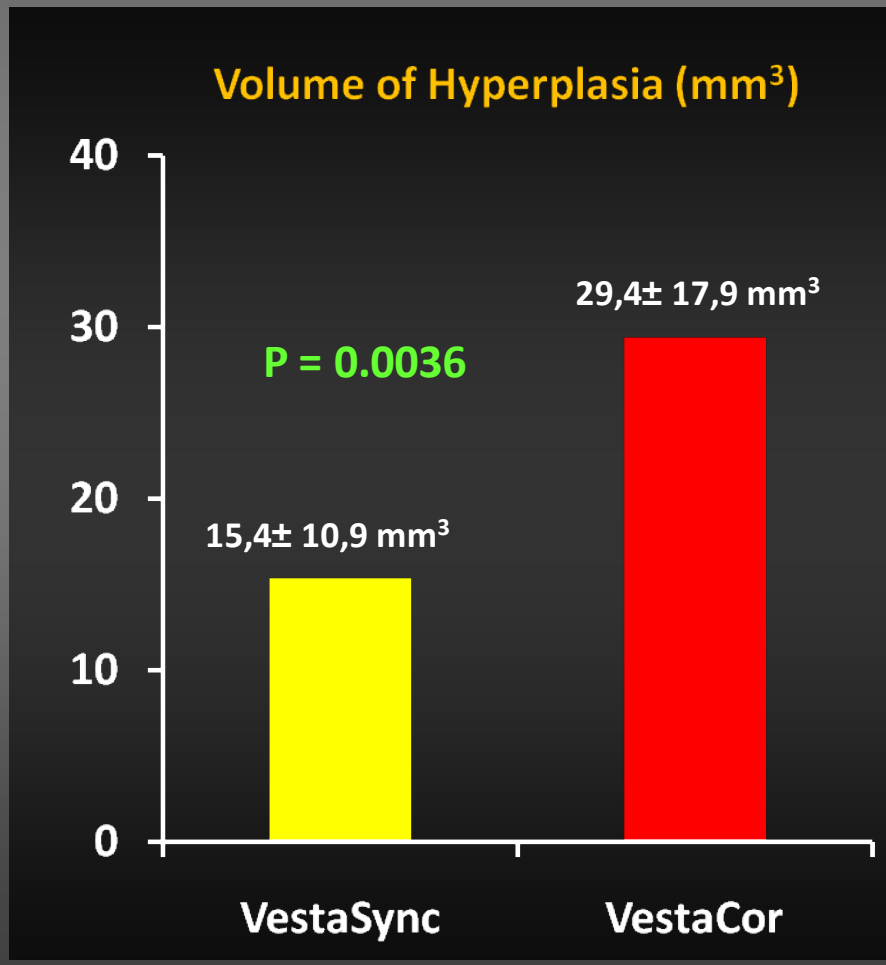


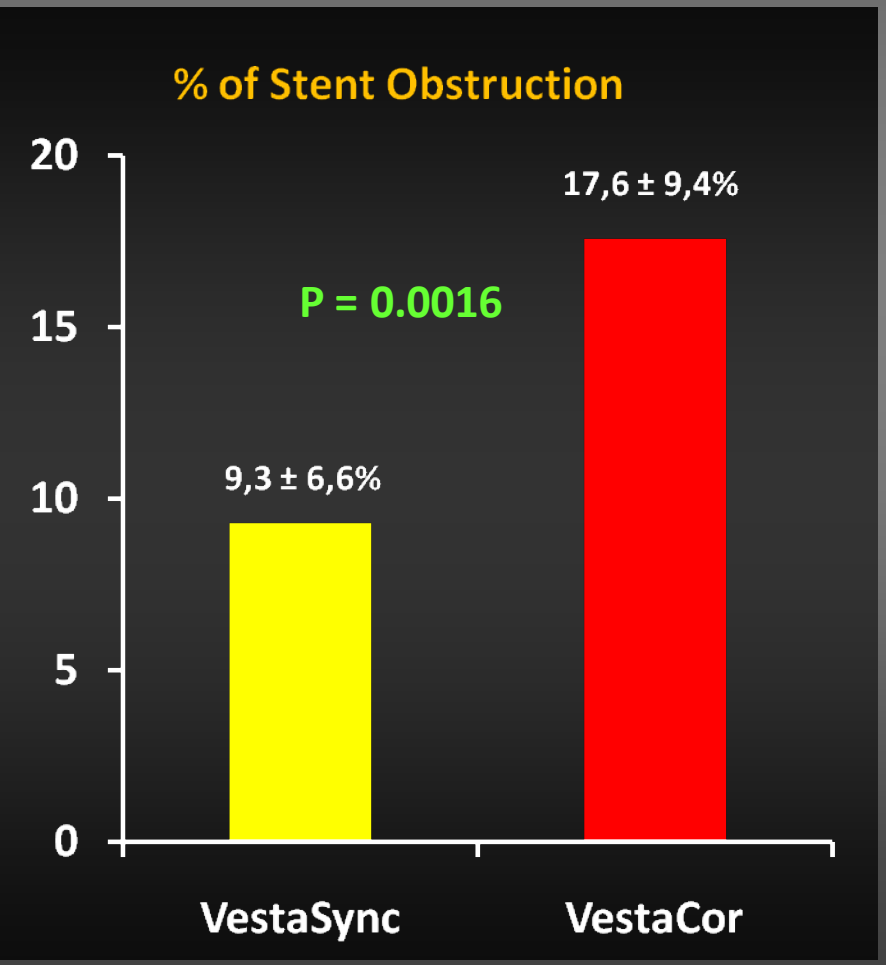
- IVUS subanalysis: 30 pts
- OCT sub-analysis : 30 pts
- Endothelial function: 20 pts

VestaSync II trial

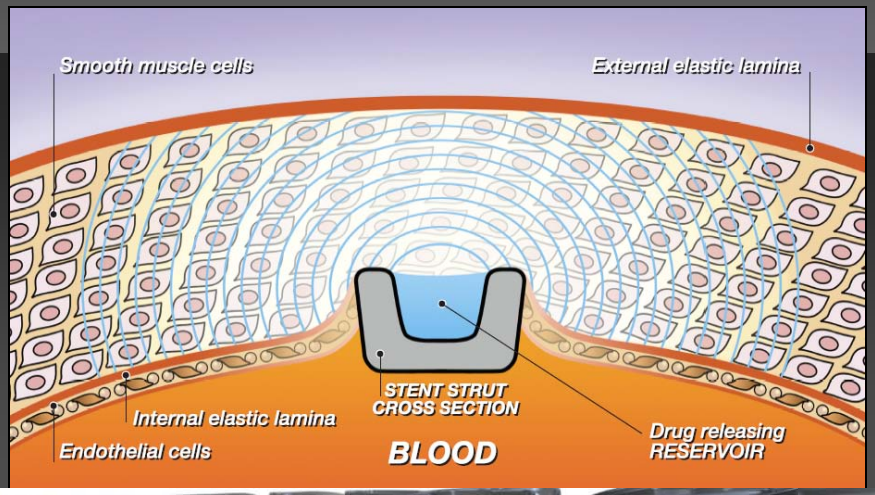


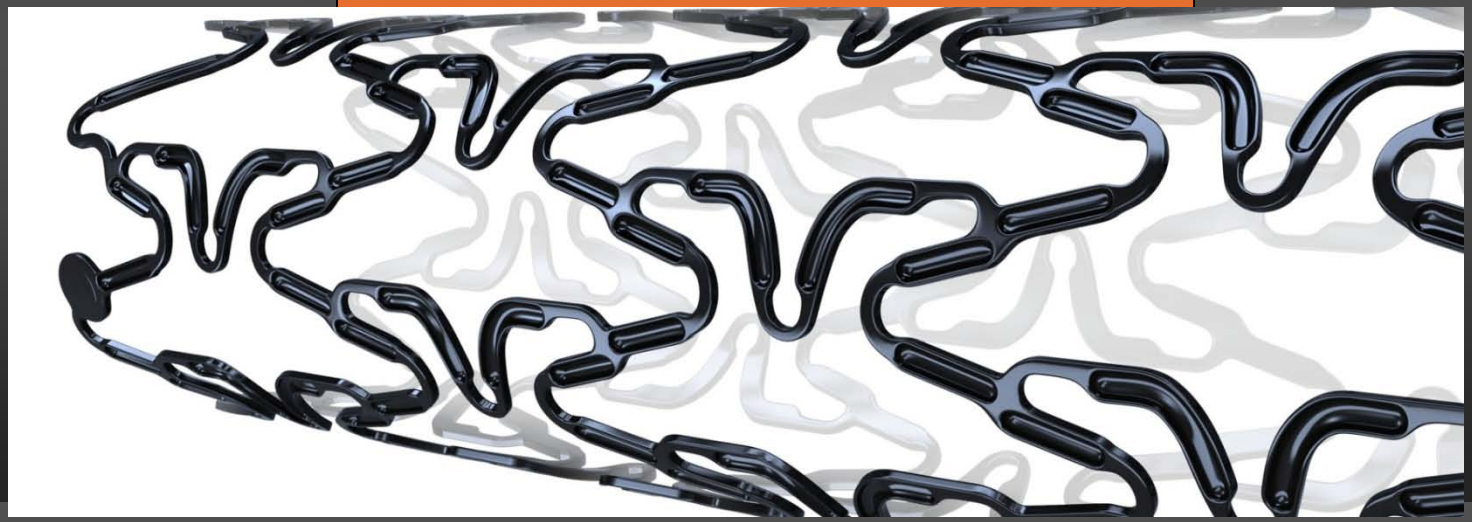
VestaSync II trial
IVUS Results





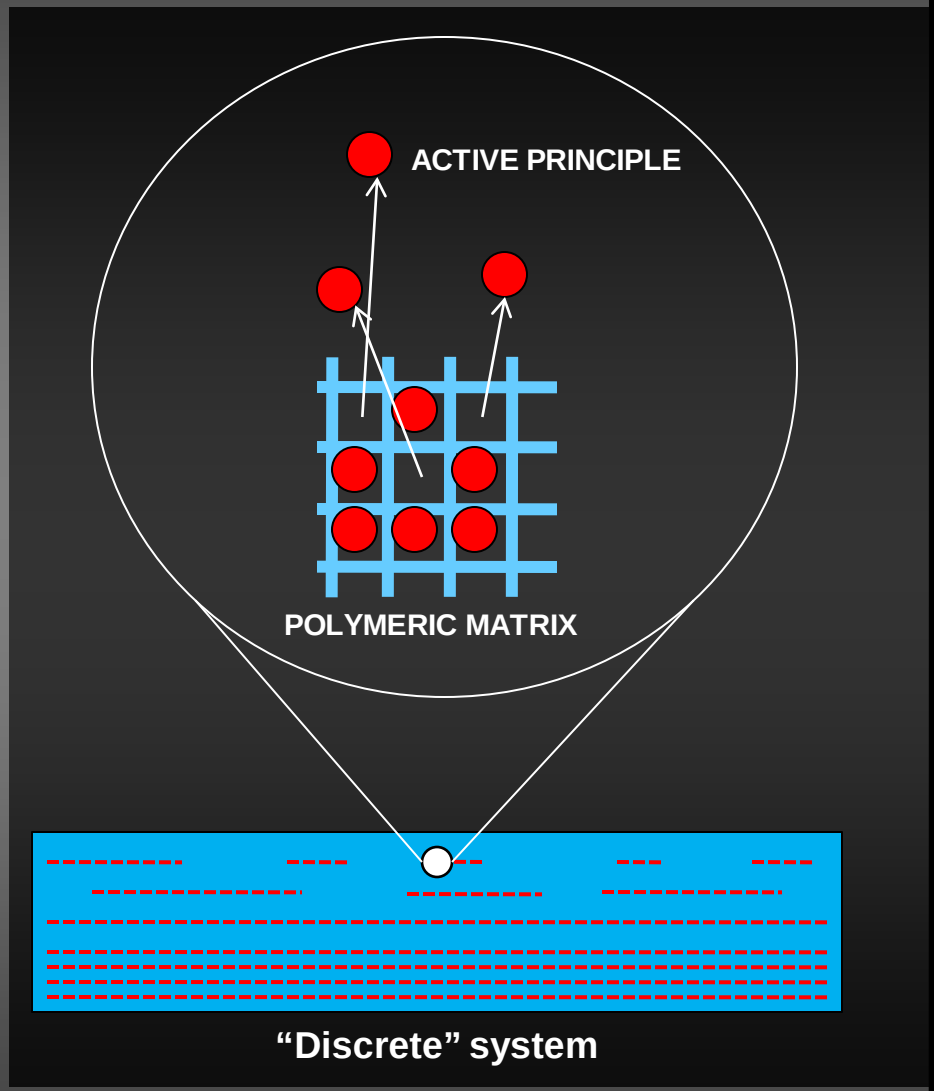
CID Polymer-free Abluminal Reservoir DES Technology





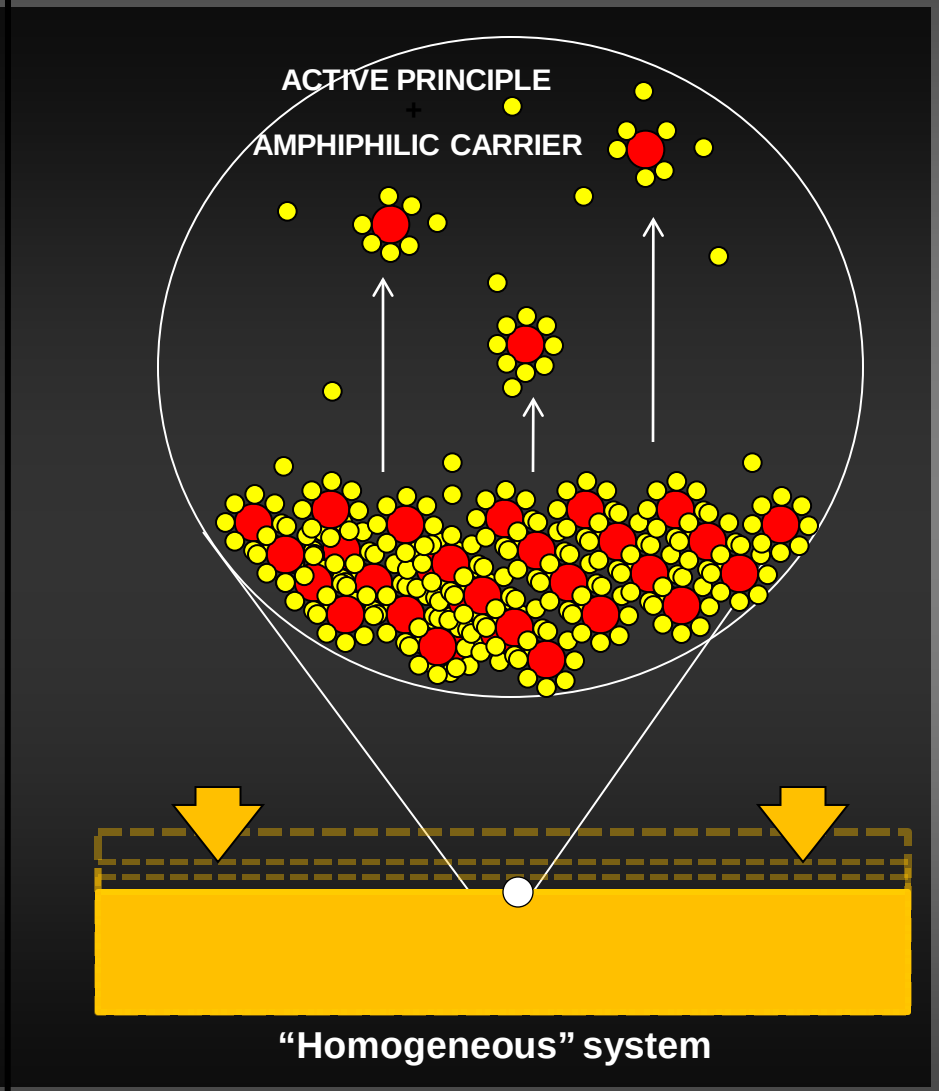
Drug Release

Polymeric Drug System



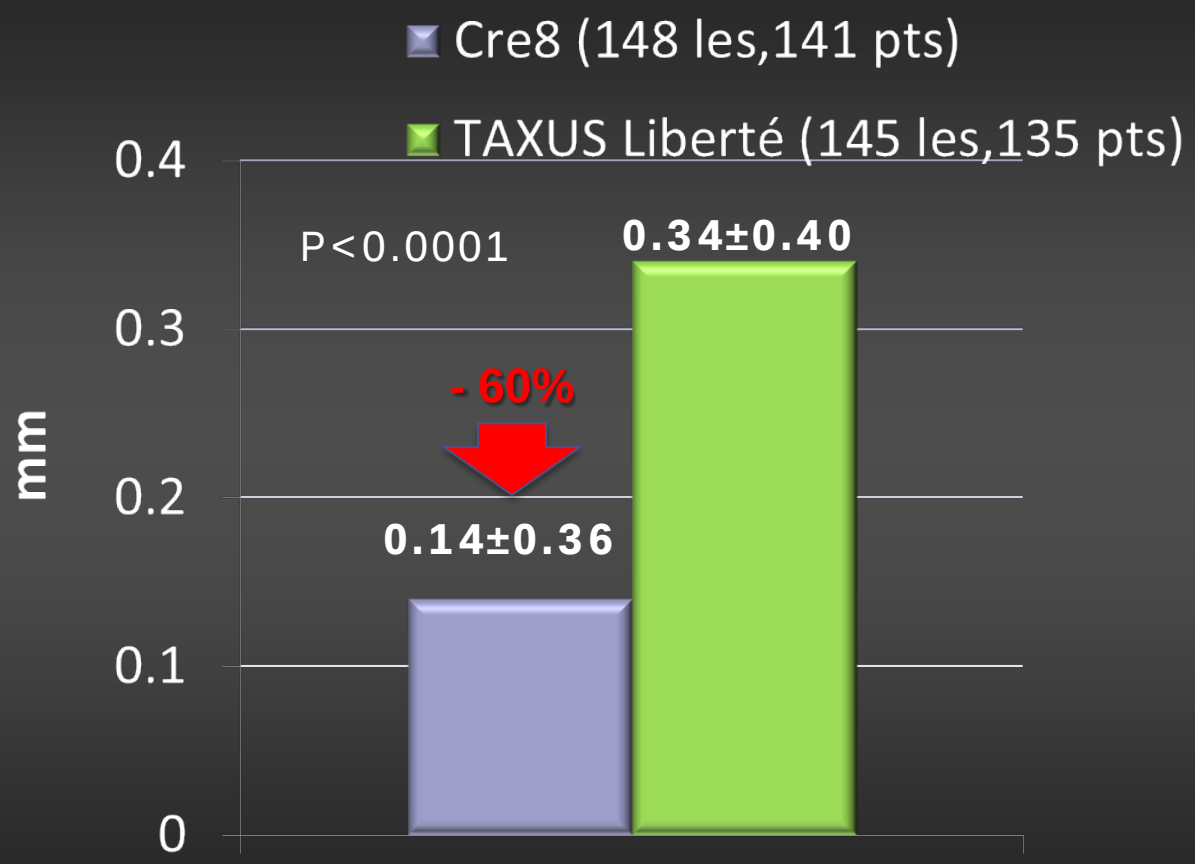
"Discrete" system

CID Amphilimus™ Formulation



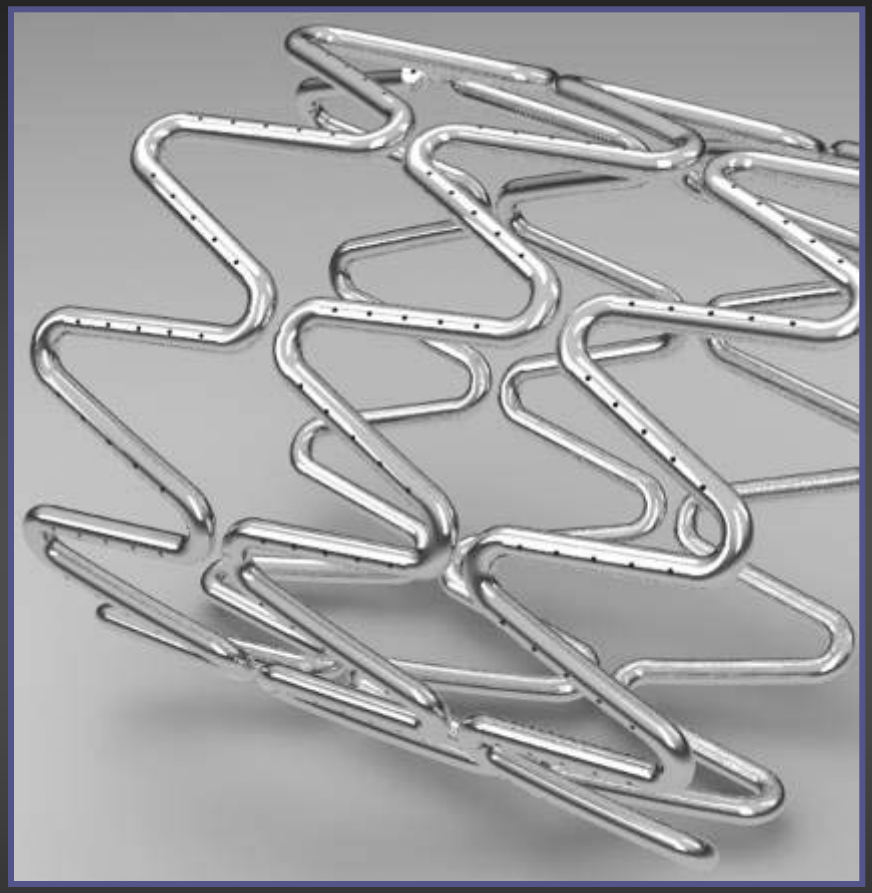
"Homogeneous" system

Primary Endpoint:
6-month in-stent Late Lumen Loss

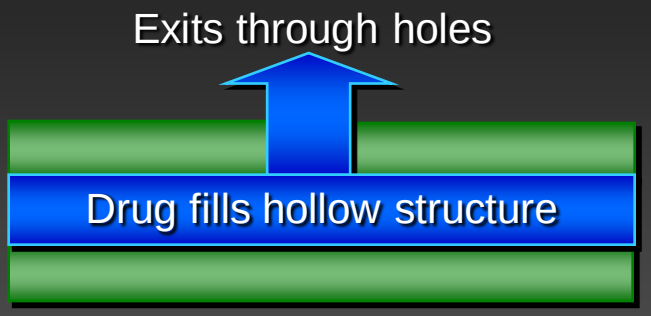


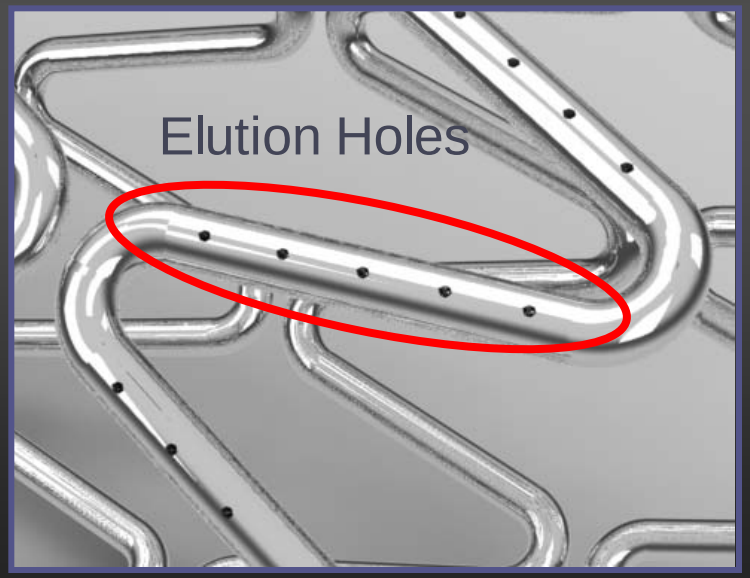
Drug Filled Stent (DFS) Concept (Medtronic)

Drug elution controlled by diffusion physics



No Polymer!





Conclusions

- First generation DES with thick and less biocompatible polymers will be gradually replaced to more advanced technology.

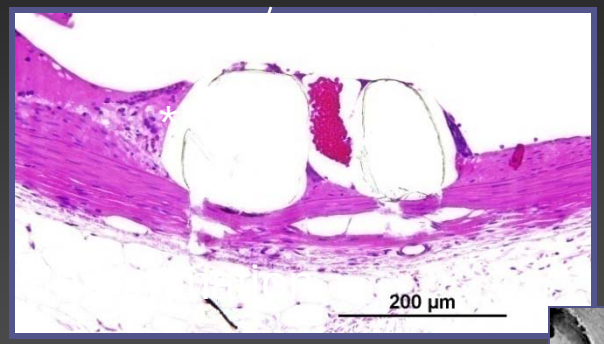
- Preliminary evidence (mainly at long-term) is showing that DES with bioabsorbable polymers might be safer that first generation devices.

- Polymer-free DES is still in early phase of research, but if confirmed in larger randomized trials it could be an attractive alternative in the future.

Instituto Dante Pazzanese de Cardiologia: Thank you

Delayed Healing - DES

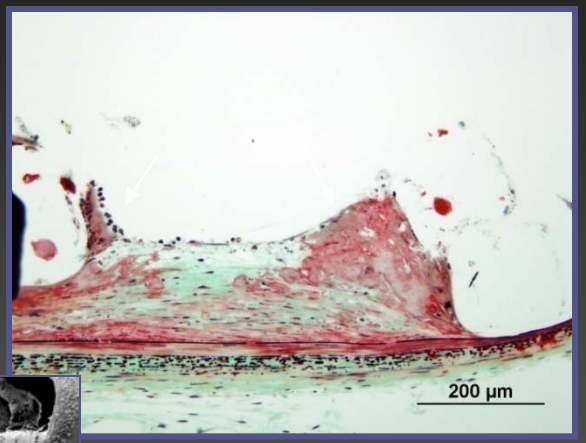
Lack of neointimal growth (uncovered Struts)



Rabbit 28 days

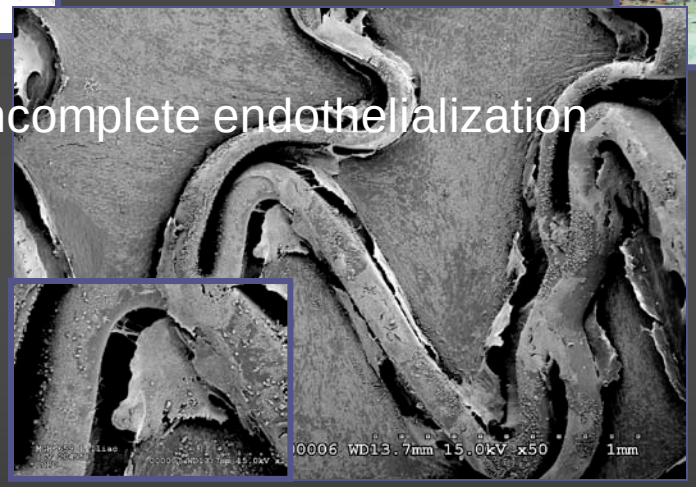
CYPHER

Persistent fibrin deposition

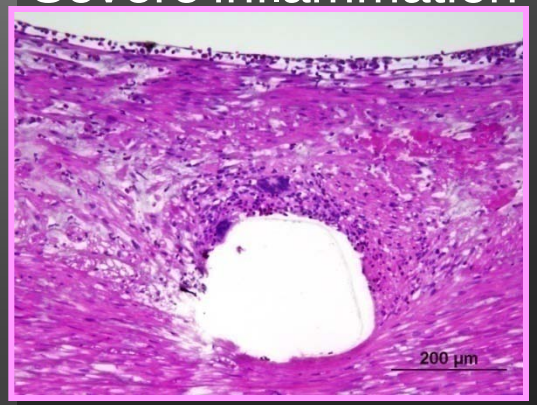


TAXUS

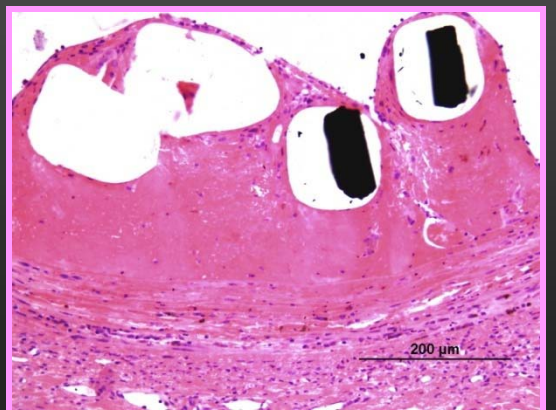
Incomplete endothelialization



Severe inflammation



Fibrin deposition with malapposition



Porcine 28 days

Virmani et al.

The FIM Team in Sao Paulo, Dec. 2000

Meril family of Trials –meriTseries

MeriT – I is a prospective, single center primary safety and efficacy trial for BioMime™ Sirolimus Eluting Coronary Stent System.

MeriT – II is a prospective, multi-centric, non-randomized, all-comers study to asses safety and efficacy of BioMime™ Sirolimus Eluting Coronary Stent System.

e - MeriT is a global post marketing surveillance study to understand the behaviour of BioMime™ Sirolimus Eluting Coronary Stent System used in routine multitude of clinical situations.