TCTAP 2011

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BIOFREEDOM: Polymer free Biolimus A9 eluting Stents and Paclitaxel eluting stents

Eberhard Grube MD, FACC, FSCAI

Hospital Oswaldo Cruz - Dante Pazzanese, São Paulo, Brazil

University Hospital Bonn, Germany

Stanford University, Palo Alto, California, USA

Financial Disclosure

Financial Relationship: Eberhard Grube MD

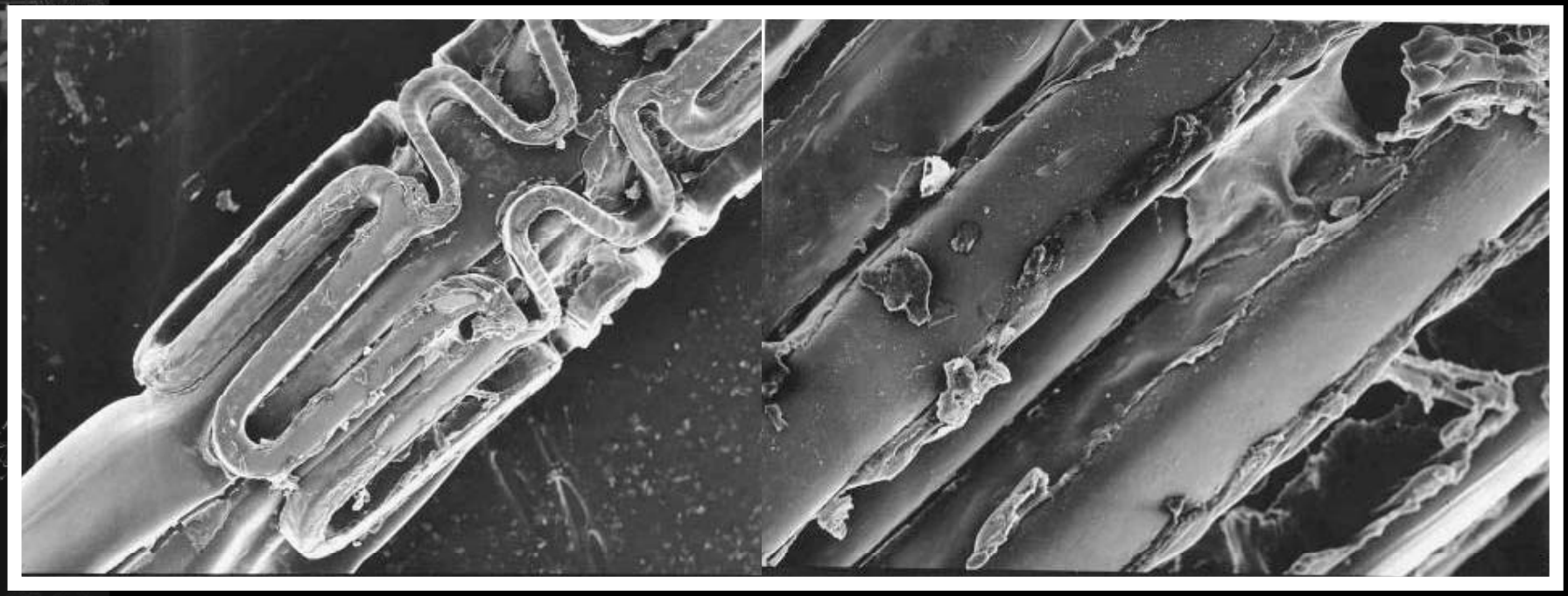
Consulting Fees/SAB:

Direct Flow, Mitralign. Boston Scientific, Medtronic Core Valve, Claret, Abbott Vascular, Cordis JnJ, Sadra,

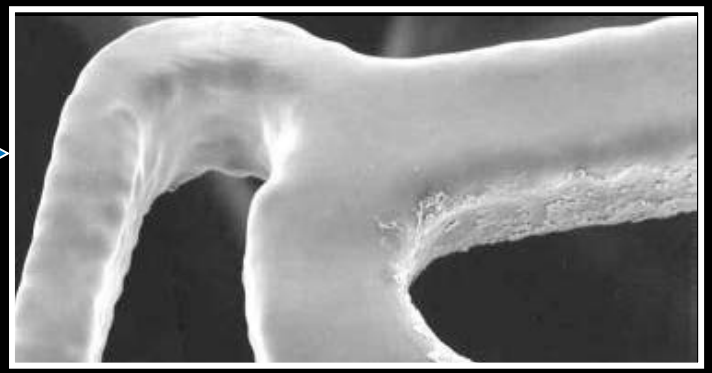
Other Financial Benefit:

Payed Proktorship Medtronic Core Valve

DES failed to cross a heavily calcified lesion…

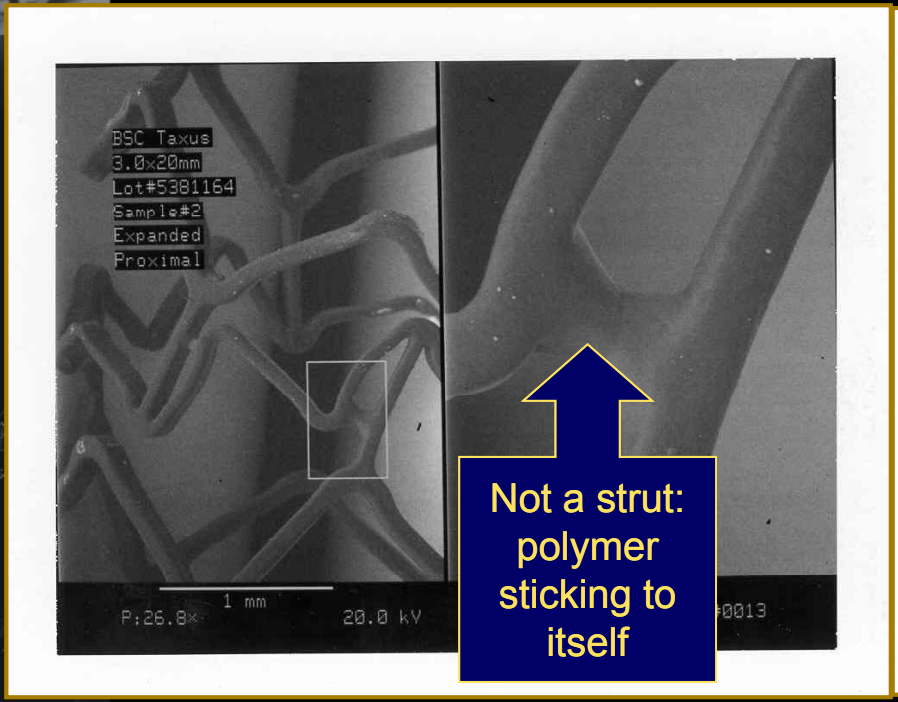


Undamaged polymer



Severe polymer damage

Polymer Mishaps: Bonding and Webbing



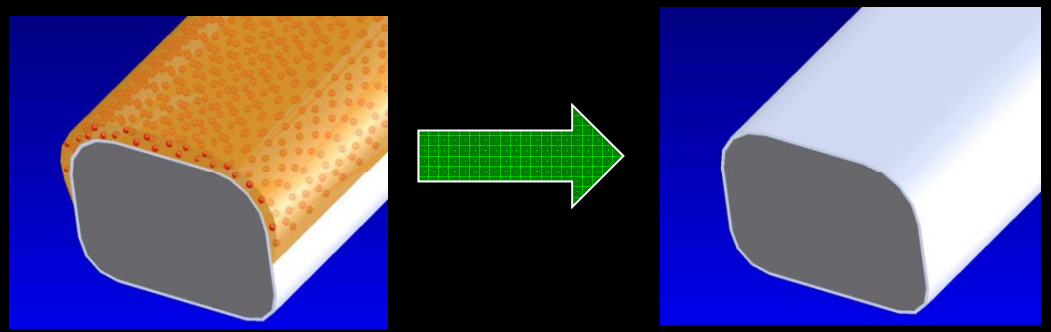
Bonding = polymer sticks to itself forming a bridge when the stent is expanded

Webbing = polymer pulling away from the expanded stent due to sticking

Bioabsorbable Drug Coatings

Concept: The role of polymer coatings is to deliver drugs in the short term and is not needed long term.

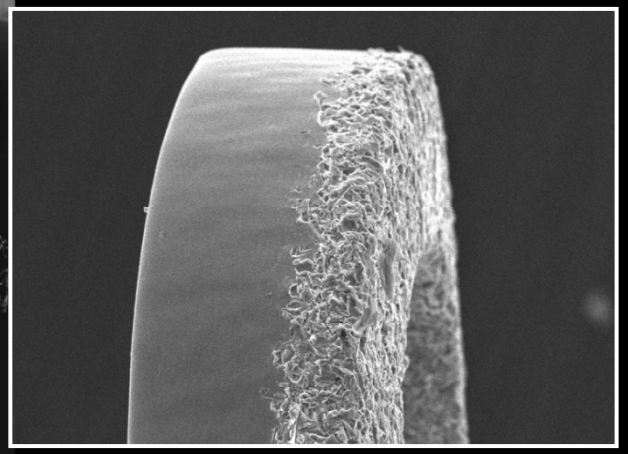
- Maintain efficacy and acute performance
- Reduce late events and DAPT requirements
  - No remaining polymer shortly after effective drug distribution
  - Minimize drug load and total coating weight



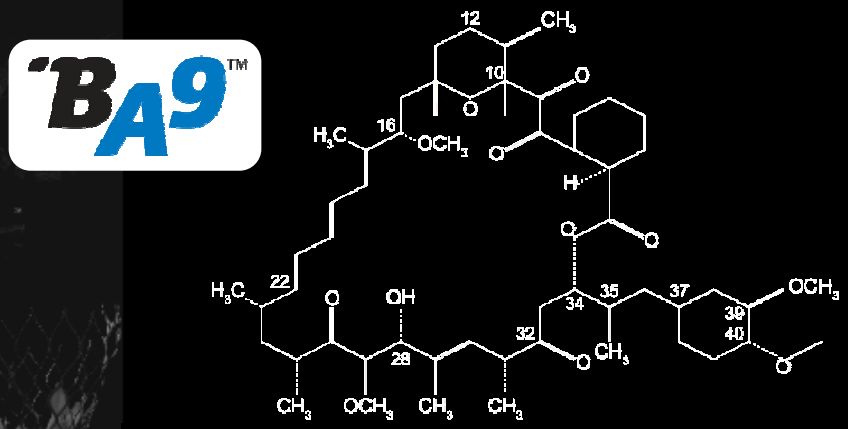
Better than any polymer is no polymer…

BioFreedom™

Selectively micro-structured surface holds drug in abluminal surface structures



Proprietary Highly Lipophilic Limus drug

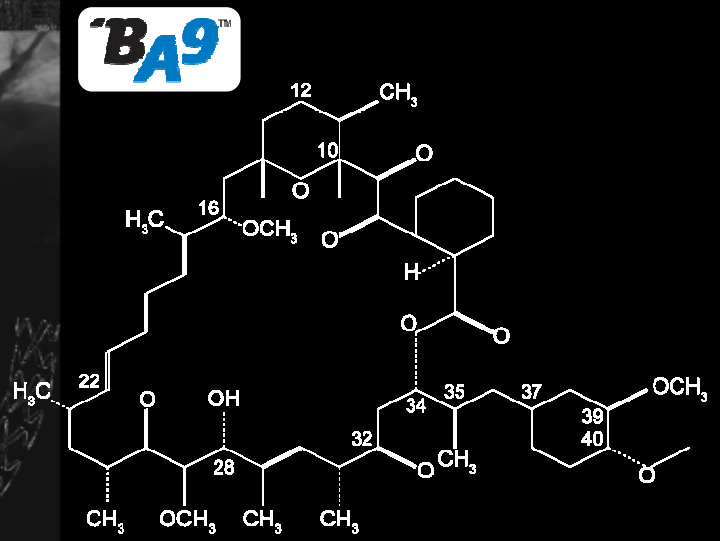


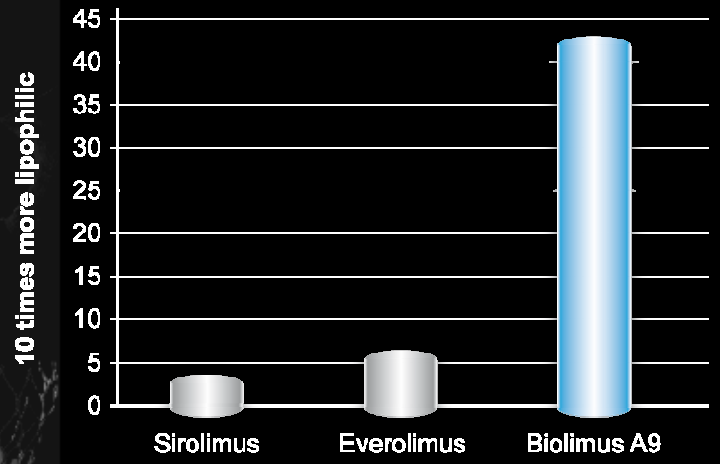
Hypothesis: Polymer-free drug release via porous-eluting stents may reduce late events caused by polymer stent coatings.

Potential advantage

- Avoid long term late adverse effects that might be attributable to the polymer
- Improved surface integrity since there is no polymer to be sheared or peeled away from the stent struts
- Possible shorter need of dual antiplatelet therapy

BIOLIMUS A9™ Drug





RAPAMYCIN DERIVATIVE

Developed specifically for stent application by Biosensors

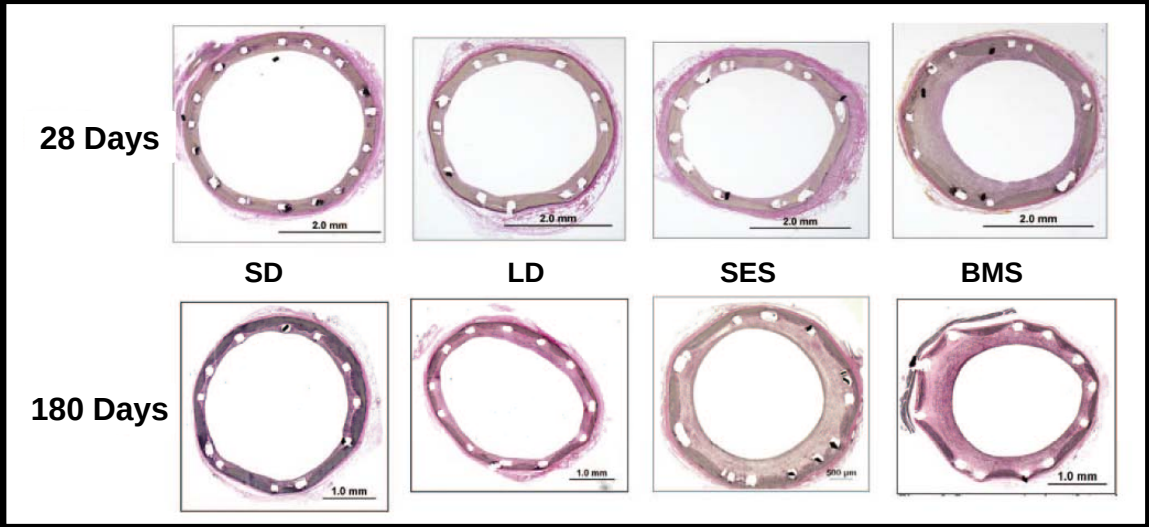
Potent immunosuppressive and anti-inflammatory properties

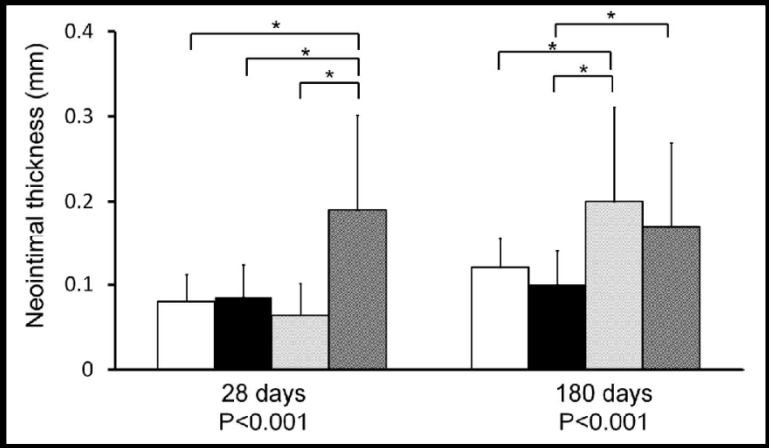
LIPOPHILICITY COMPARISON

Highest lipophilic and hydrophobic properties of commercially available limus drugs

Mainly localized effects, minimal drug release into bloodstream

Pre-Clinical Study - Efficacy
BES vs. SES & BMS

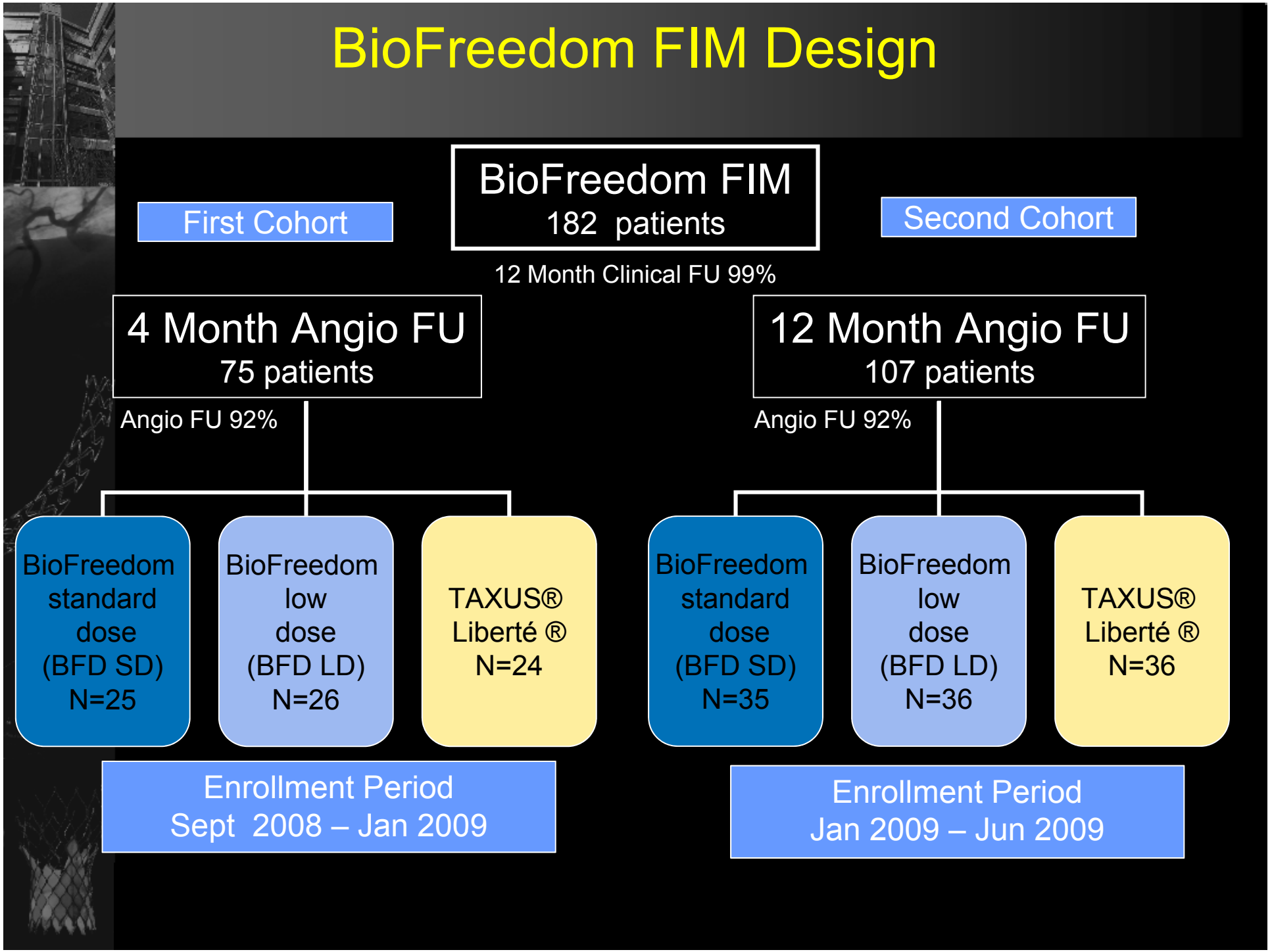




	n	28 days	180 days
□	Standard dose Bio-freedom	24	23
■	Low dose Bio-freedom	26	27
□	Sirolimus-eluting stents	30	39
■	Bare metal stents	24	24

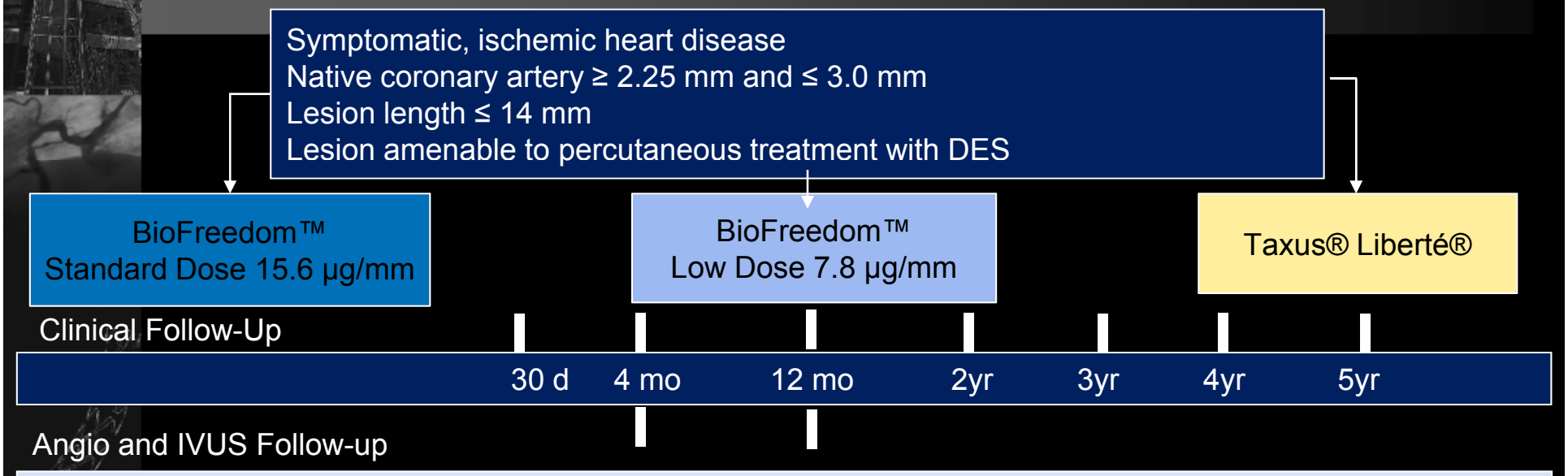
Tada et al., Circ Cardiovasc Interv 2010;3;174-183

BioFreedom FIM Design



BioFreedom FIM Study Design

Symptomatic, ischemic heart disease
Native coronary artery ≥ 2.25 mm and ≤ 3.0 mm
Lesion length ≤ 14 mm
Lesion amenable to percutaneous treatment with DES



Primary Endpoint: In-stent Late Lumen Loss (LL) at 12 months (2nd cohort)
Non-Inferiority, margin = 0.24 mm

Secondary Endpoints: In-stent Late Lumen Loss (LL) at 4 months (1st cohort)
MACE and stent thrombosis rate at 30 days, 4, 12 months, 2, 3, 4 & 5 yrs
Clinically-driven TLR, TVR and TVF at 4, 12 months, 2, 3, 4 & 5 yrs
In-stent/In-segment binary restenosis at 4 months (1st cohort) & 12 months (2nd cohort)
In-stent/In-segment Minimum Lumen Diameter (MLD) at 4 months
Neointimal hyperplasia volume (IVUS) at 4 months (1st cohort) & 12 months (2nd cohort)
Biolimus A9 concentrations pre/post procedure at discharge & 30 days

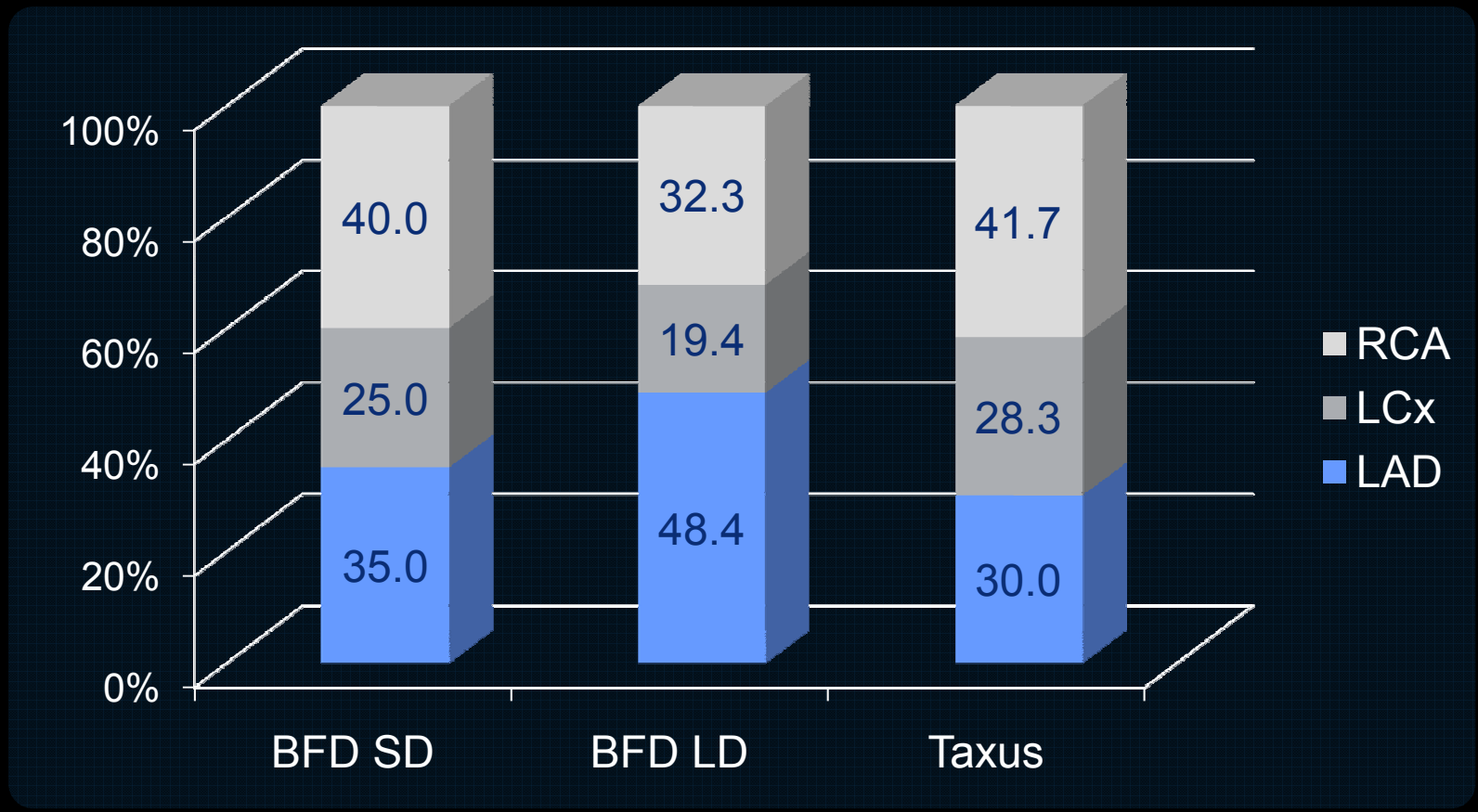
DAPT recommended for a minimum of 6 months

Patient Characteristics
All Patients (1st + 2nd Cohorts)

	BFD SD N = 60	BFD LD N = 62	Taxus N = 60
Age (mean ± SD)	68.6 ± 9.0	65.0 ± 9.4	67.9 ± 8.0
Male (%)	67	76	67
Diabetes mellitus (%)	28	29	25
Current Smoker (%)	17	20	12
Hypertension (%)	90	81	85
Hypercholesterolemia (%)	68	74	75
Previous MI (%)	20	21	18
Previous PCI (%)	32	44	46
Unstable angina (%)	12	13	7

All P values are non-significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

Lesion Location
All Patients (1st + 2nd Cohorts)



BFD LD LAD vs. Taxus LAD P=0.04. All other P values are non-significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

Procedural Characteristics
All Patients (1st + 2nd Cohorts)

	BFD SD N = 60	BFD LD N = 62	Taxus N = 60
Stents per Patient (mean ± SD)	1.1 ± 0.3	1.1 ± 0.3	1.1 ± 0.2
Pre-procedure Dilation (%)	88	92	92
Post-procedure Dilation (%)	18	23	22
Final TIMI 3 Flow (%)	100	100	100
Device Success (%)	97	100	100
Lesion Success (%)	100	100	100
Procedure Success (%)	100	98*	100

Device Success = Attainment of <50% residual stenosis of the target lesion with the study device and delivery system
Lesion Success = Attainment of <50% residual stenosis of the target lesion using any percutaneous method
Procedure Success = Attainment of <50% residual stenosis of the target lesion and no in-hospital MACE

*Peri-procedural Non-Q wave MI

All P values are non -significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

Pre- Procedural QCA
All Lesions (1st + 2nd Cohorts)

	BFD SD N = 59	BFD LD N = 63	Taxus N = 60
RVD (mm)	2.8 [2.5, 3.0]	2.8 [2.5, 3.0]	2.8 [2.5, 3.0]
MLD (mm)	0.6 [0.3, 0.9]	0.6 [0.4, 0.9]	0.7 [0.5, 0.9]
% DS	76.0 [64.3, 87.6]	77.2 [67.0, 85.8]	75.9 [67.2, 83.6]
Lesion length (mm)	10.6 [9.3, 13.9]	11.3 [9.8, 13.6]	11.2 [9.5, 14.0]

All values are presented as median [IQR].
All P values are non significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

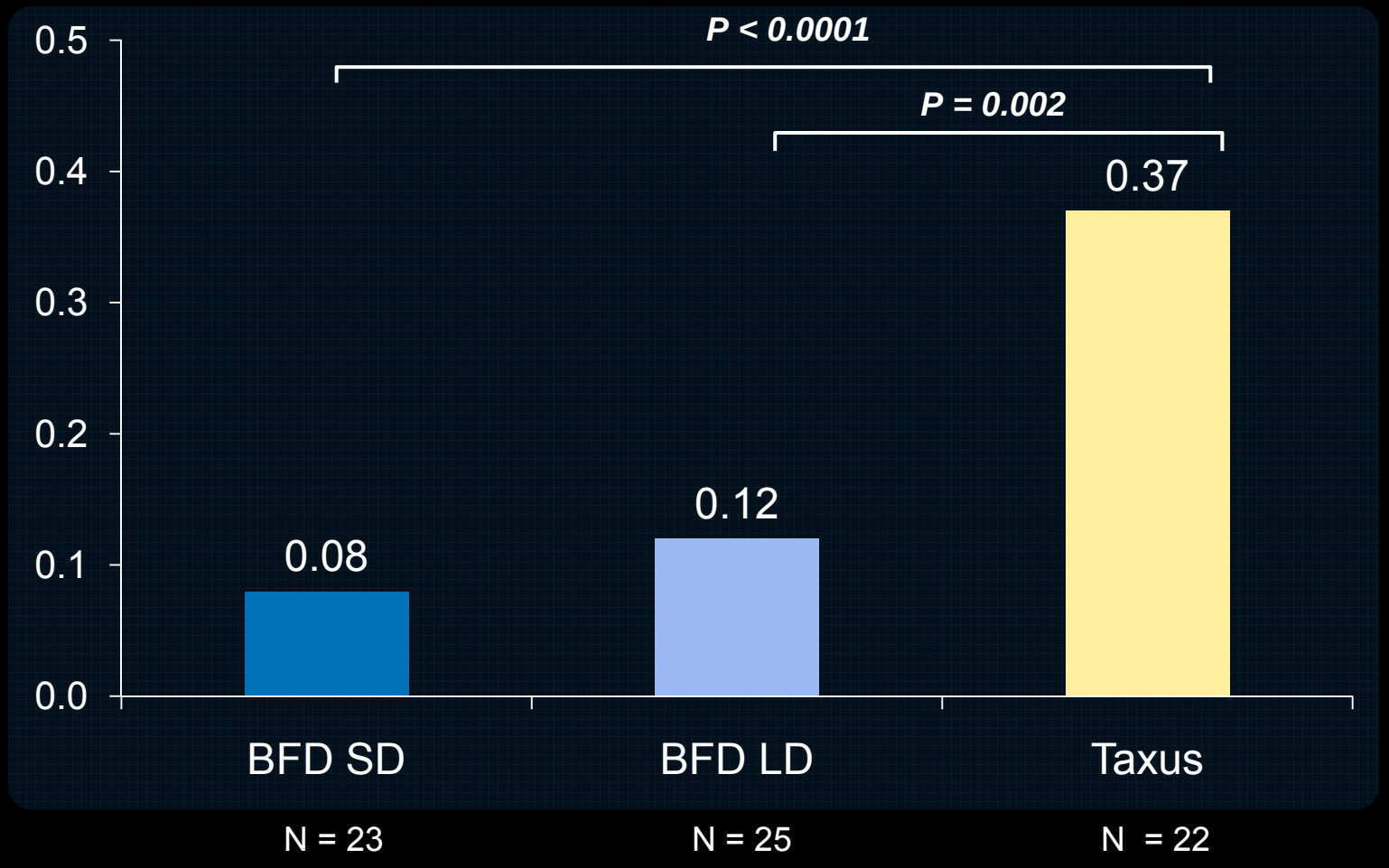
Post- Procedural QCA
All Lesions (1st + 2nd Cohorts)

	BFD SD N = 59	BFD LD N = 63	Taxus N = 60
Acute Gain (mm)			
In-segment	1.6 [1.3, 2.0]	1.6 [1.4, 1.8]	1.6 [1.3, 2.0]
In-stent	2.0 [1.6, 2.2]	1.9 [1.7, 2.2]	1.9 [1.7, 2.2]
MLD (mm)			
In-segment	2.3 [2.0, 2.5]	2.2 [2.1, 2.5]	2.2 [2.0, 2.6]
In-stent	2.7 [2.3, 2.8]	2.6 [2.3, 2.8]	2.6 [2.4, 2.8]
% Diameter Stenosis			
In-segment	17.2 [9.4, 24.3]	16.9 [12.0, 23.0]	19.1 [12.0, 24.0]
In-stent	6.2 [3.9, 11.5]	7.4 [4.5, 9.9]	6.1 [3.6, 9.4]

All values are presented as median [IQR]. All P values are non-significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

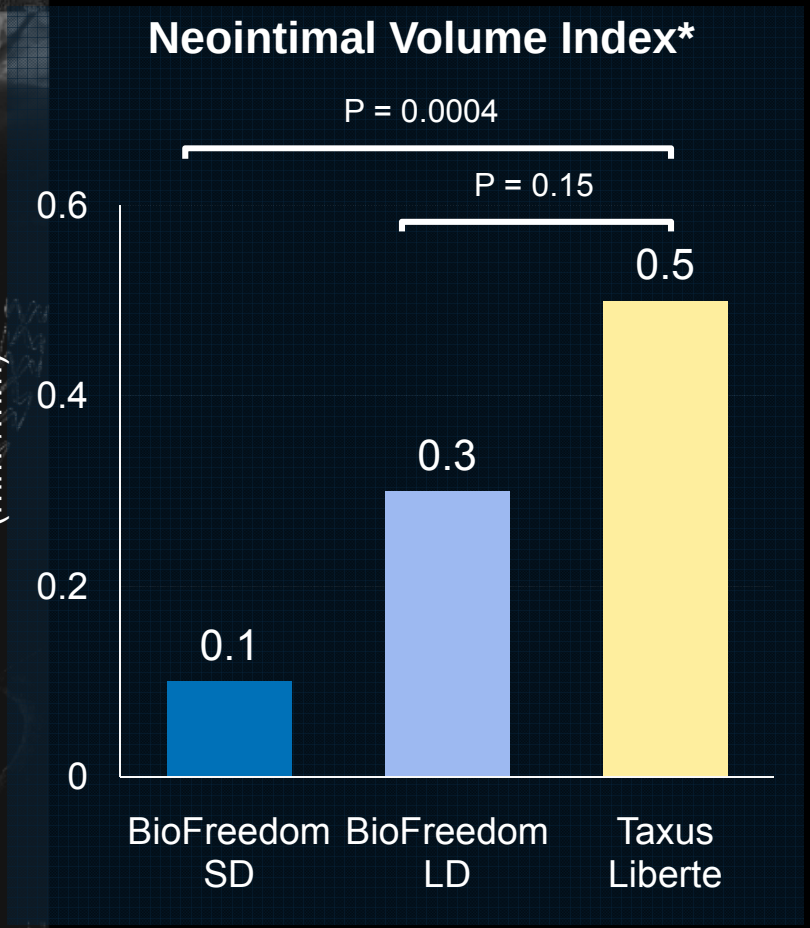
4 Month Angiographic FU
In-Stent Late Lumen Loss: 1st Cohort

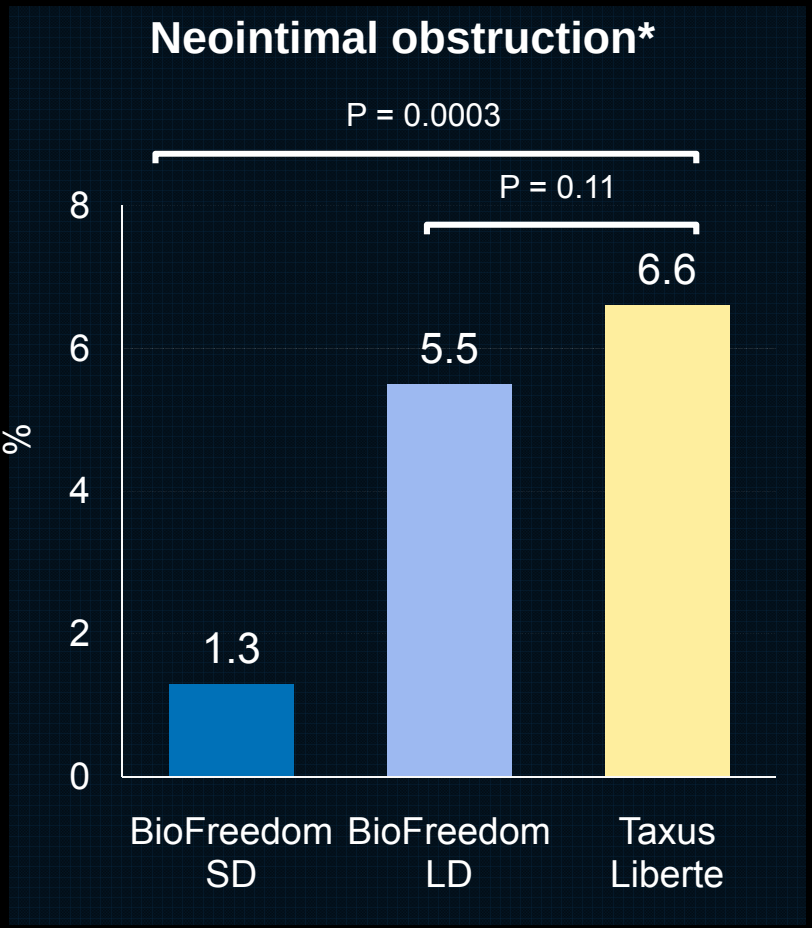
Secondary Endpoint



All values are presented as median.
Grube E., oral presentation, TCT 2009

4-Month IVUS FU
1st Cohort





Follow-up 3D IVUS analysis: n=44

*median values

Grube E., oral presentation, TCT 2009

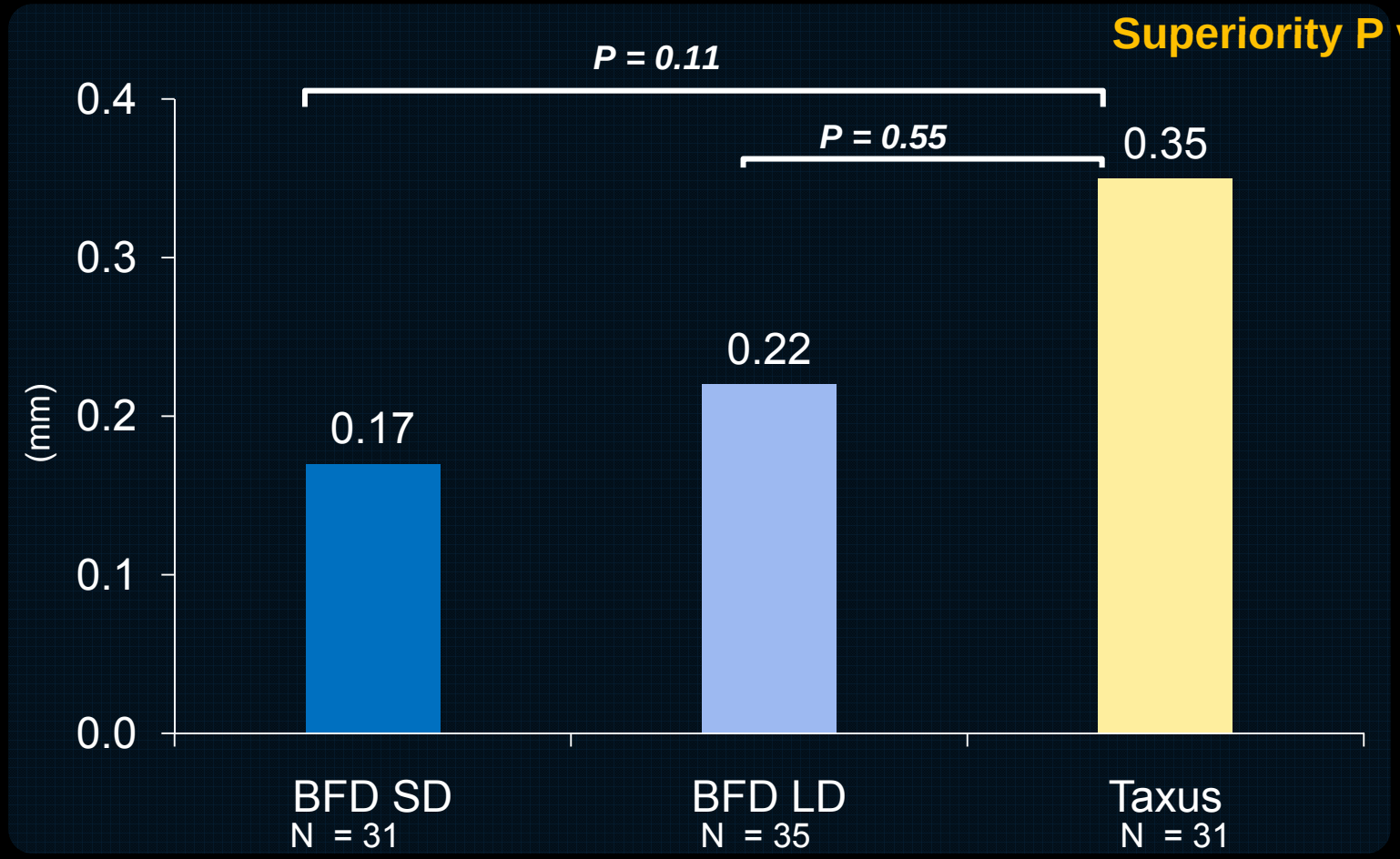
12 Month Angiographic FU
2nd Cohort

	BFD SD N = 31	BFD LD N = 35	Taxus N = 31
MLD (mm)			
In-segment	2.1 [1.9, 2.4]	2.0 [1.6, 2.3]	2.0 [1.9, 2.3]
In-stent	2.4 [2.0, 2.6]	2.2 [1.8, 2.6]	2.3 [2.0, 2.4]
% Diameter Stenosis			
In-segment	21.8 [14.6, 30.9]	23.7 [15.0, 45.0]	22.9 [17.1, 32.9]
In-stent	13.8 [9.4, 21.3]	13.6 [9.0, 39.5]	19.3 [10.0, 25.0]

All values are presented as median [IQR]. All P values are non significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

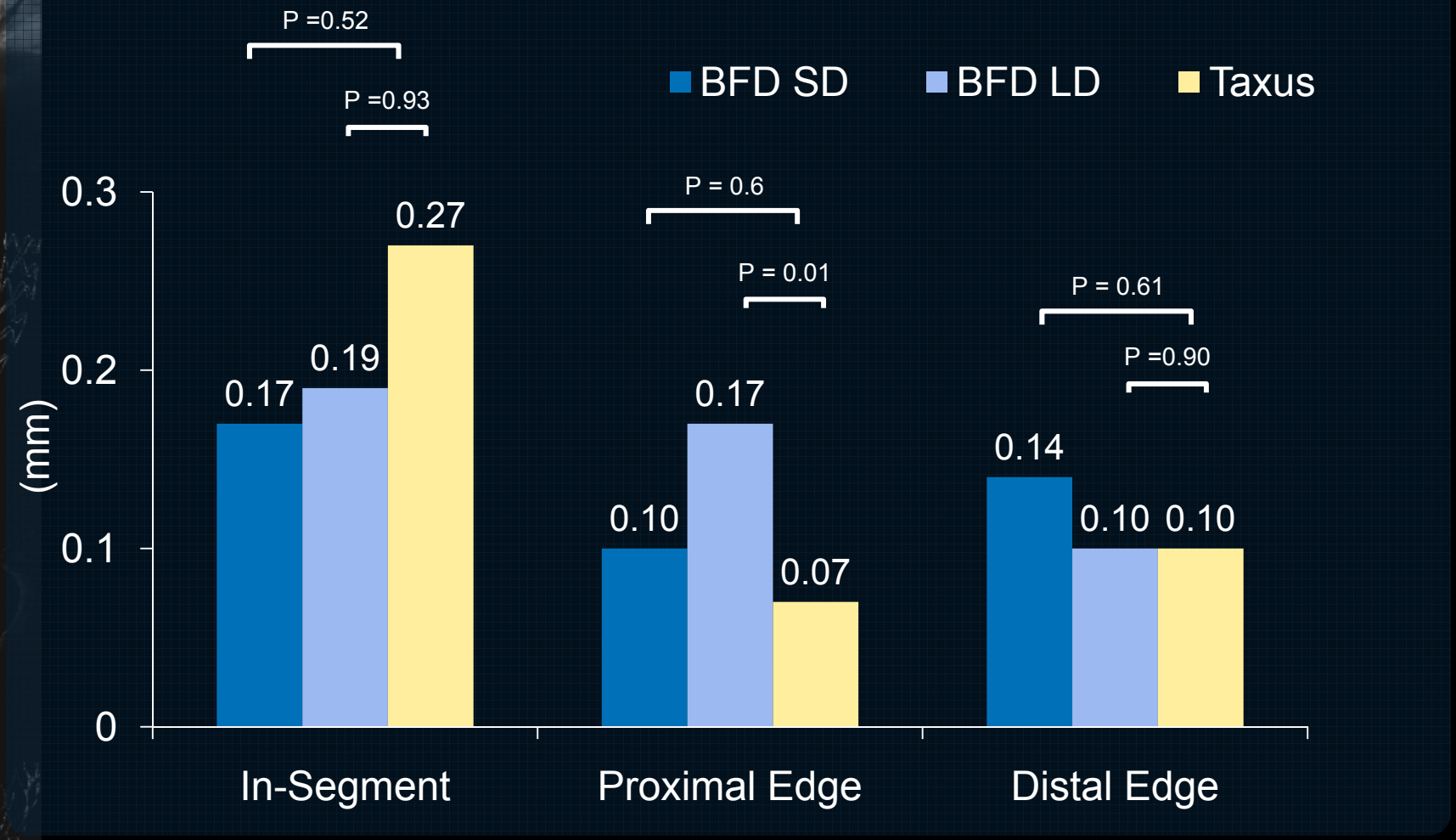
12 Month Angiographic FU
In-Stent Late Lumen Loss: 2nd Cohort

Primary Endpoint



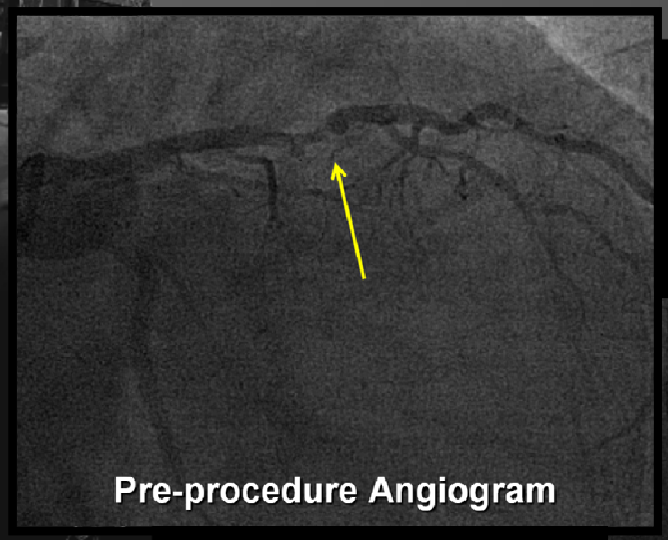
All values are presented as median.

12 Month Angiographic FU
Late Lumen Loss: 2nd Cohort

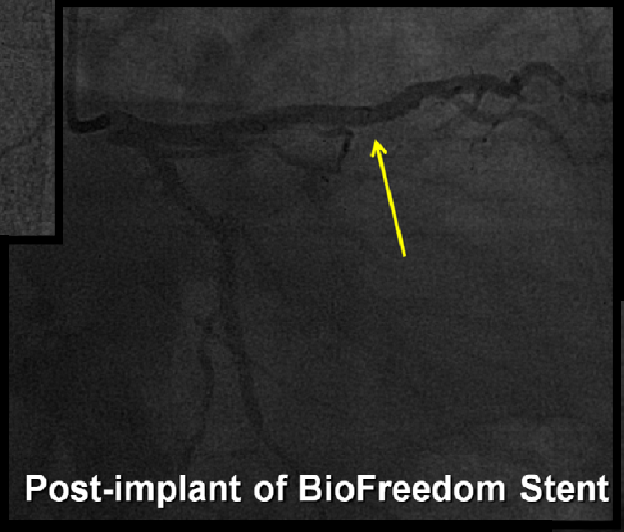


All values are presented as medians.
All P-values are caluculated for superiority.

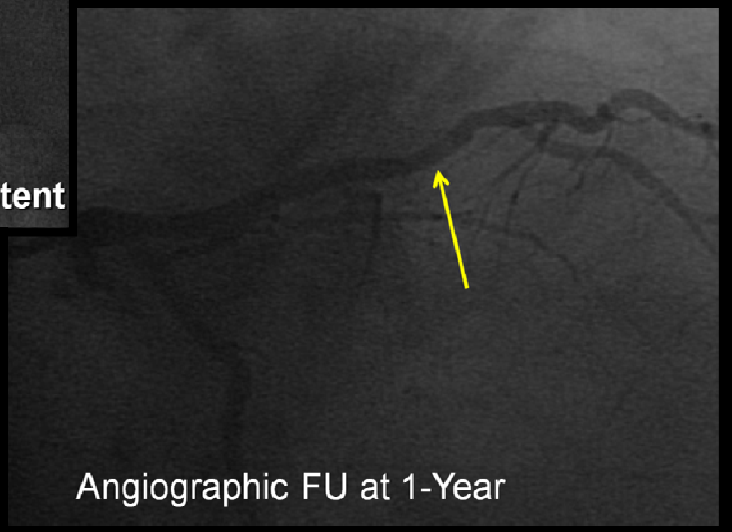
Case Example BioFreedom SD



Pre-procedure Angiogram

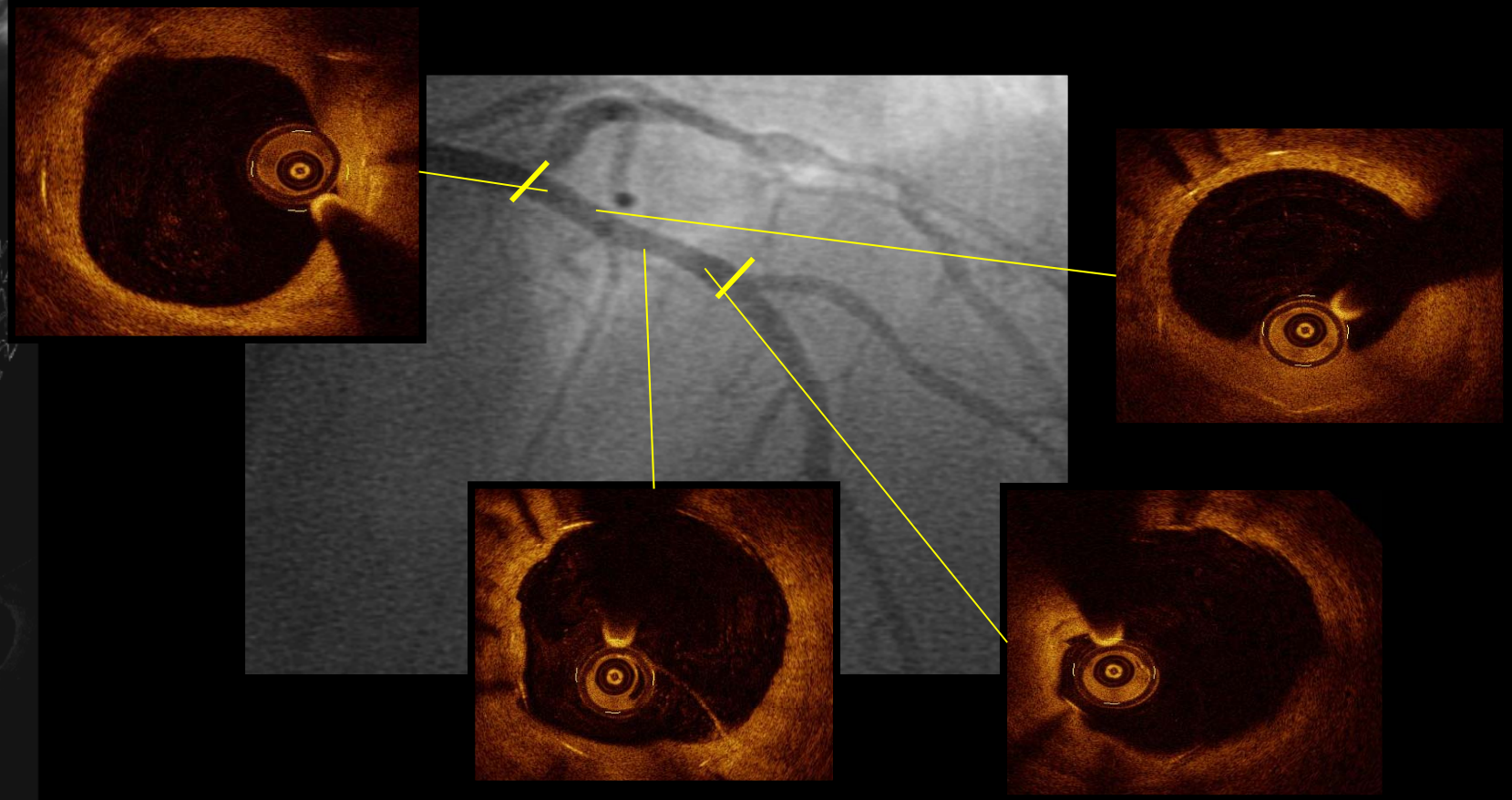


Post-implant of BioFreedom Stent



Angiographic FU at 1-Year

Case Example BioFreedom SD
OCT Evaluation at 1 Year FU



12 Month MACE – (KM Estimates)
All Patients (1st + 2nd Cohorts)

	BFD SD N = 60	BFD LD N = 62	Taxus N = 60
MACE* (All Death, MI, Emergent Bypass or TLR)	3 (6.1%)	7 (11.6%)	3 (5.5%)
All Death	1 (1.8%)	0 (0.0%)	0 (0.0%)
MI	1 (1.8%)	1 (1.6%)	0 (0.0%)
Q Wave MI	0 (0.0%)	0 (0.0%)	0 (0.0%)
Non-Q Wave MI	1 (1.8%)	1 (1.6%)**	0 (0.0%)
Emergent Bypass	0 (0.0%)	0 (0.0%)	0 (0.0%)
TLR	1 (1.8%)	6 (10.0%)	3 (5.5%)

*Time to first event
**In-hospital MI

All p values are non significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

12 Month Stent Thrombosis
All Patients (1st + 2nd Cohorts)

	BFD SD N = 60	BFD LD N = 62	Taxus N = 60
Acute (%)	0	0	0
Sub-acute (%)	0	0	0
Late (%)	0	0	0

Possible, probable or definite stent thrombosis as per ARC Definition.

All P values are non significant.
Tests were performed for BFD SD vs. Taxus and BFD LD vs. Taxus.

Summary & Conclusions - 1

- Primary endpoint (In-Stent LL at 12 months) met: BioFreedom SD non-inferior to Taxus.
- In-Stent LL for BioFreedom SD (0.17 mm) demonstrated a trend towards superiority at 12 months compared to Taxus (0.35 mm).
- Both BioFreedom SD and BioFreedom LD demonstrated sustained safety up to 12 months, including absence of stent thrombosis.

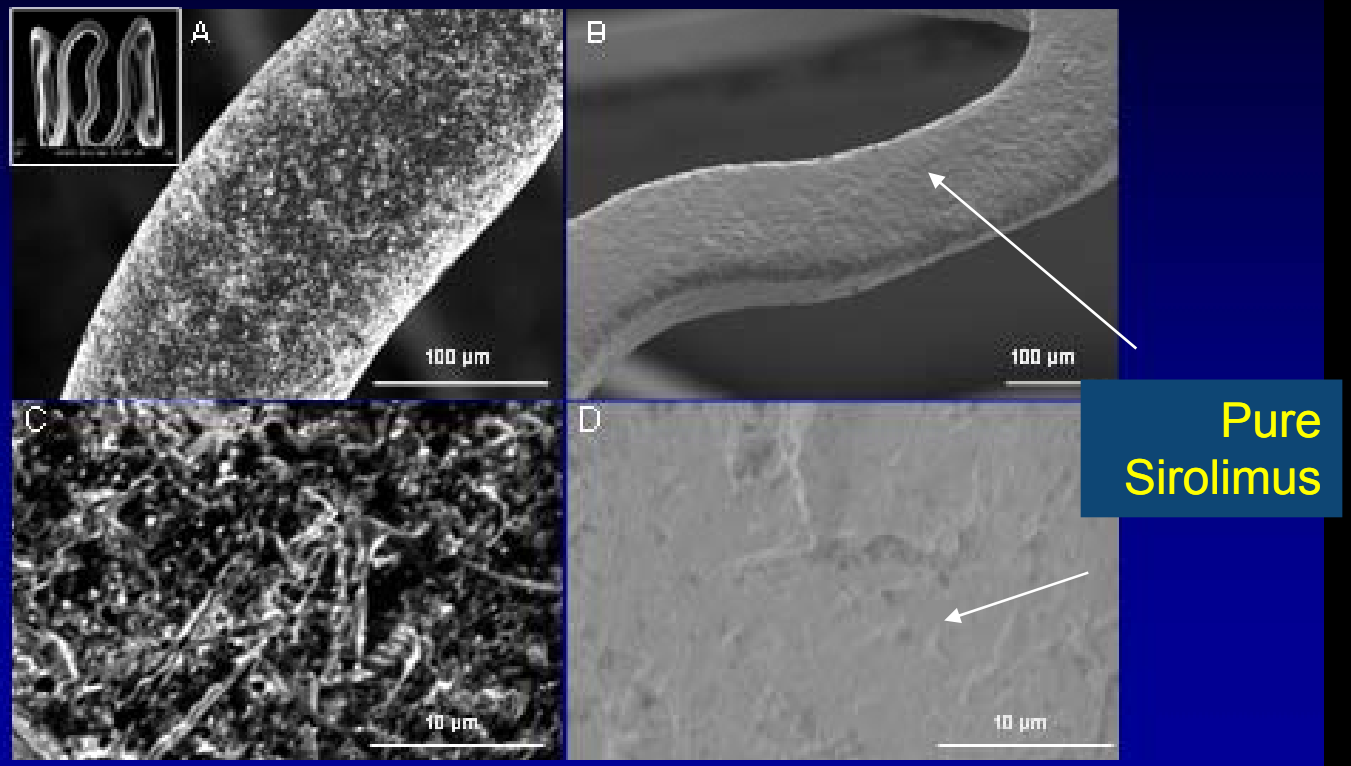
Summary & Conclusions - 2

- BioFreedom: first polymer-free drug coated stent demonstrating comparable efficacy in inhibiting NIH (as assessed by independent QCA analysis) vs. a currently available DES with durable polymer at 12 months in a randomized clinical trial.

- Larger trial with longer term follow-up warranted to confirm these encouraging results.

Translumina Porous Surface Stent

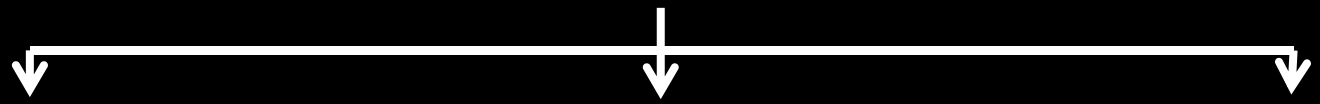
Unique microporous stent surface



before coating after

ISAR-TEST 3:
Testing Different Sirolimus-Coating Strategies

605 pts with de-novo lesions randomized



polymer-free	biodegradable polymer	durable polymer (Cypher)
(n=201)	(n=202)	(n=202)

Primary Endpoint: in-stent late lumen loss (non-inferiority trial)

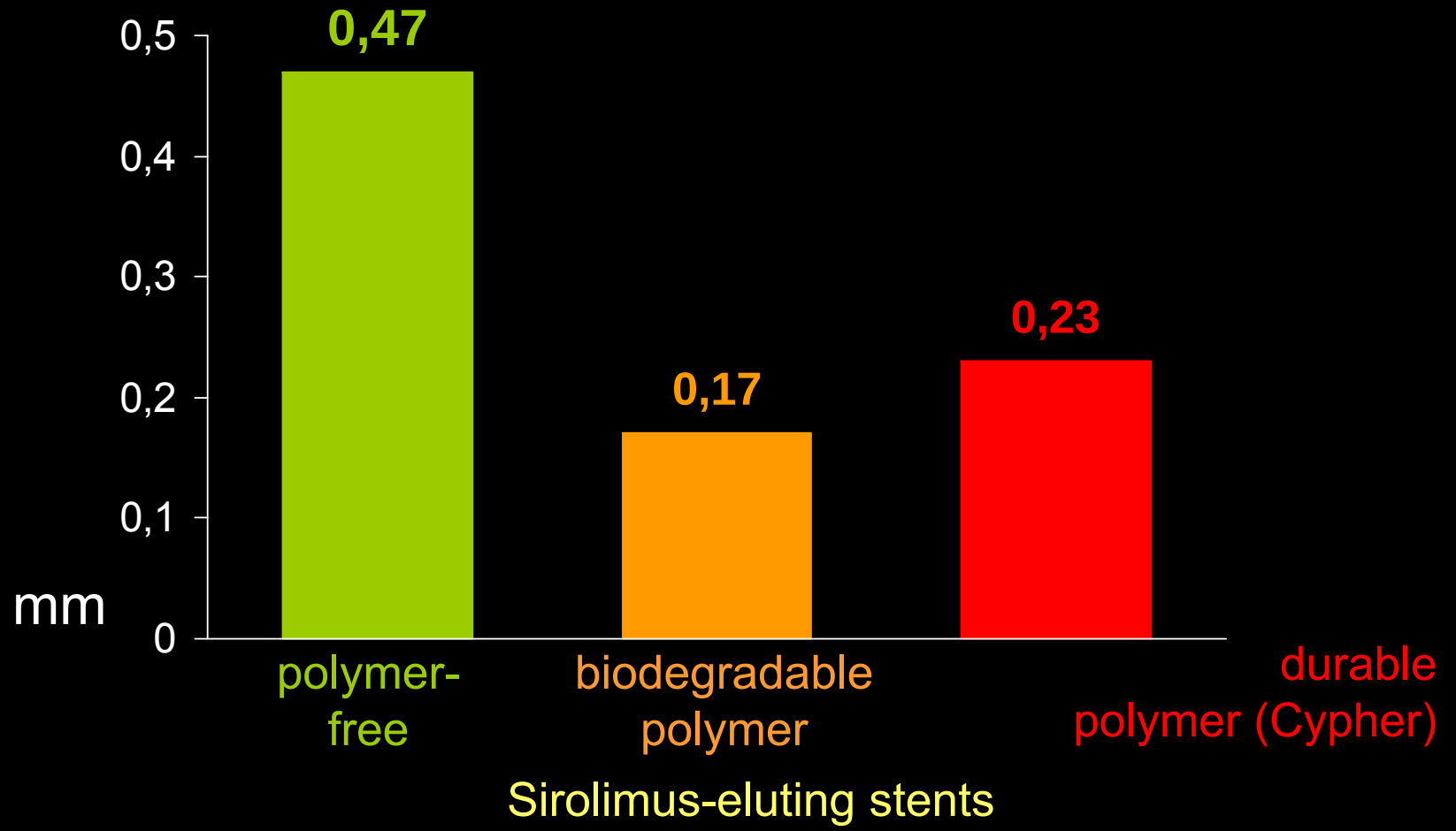
Secondary Endpoint: binary restenosis rate, clinical events at 1 yr.

J Mehilli et al., *Eur Heart J* 2008

ISAR-TEST 3:

Less Efficacy with Non-Polymer vs. Polymer-Based SES

Primary EP: In-Stent Late Lumen Loss at FU



J Mehilli et al., *Eur Heart J* 2008

Polymer Free Paclitaxel

§ Abluminal coating – 5µ thickness applied on crimped stent.

§ Consistent coating ensuring 98% of the drug delivered to the site.

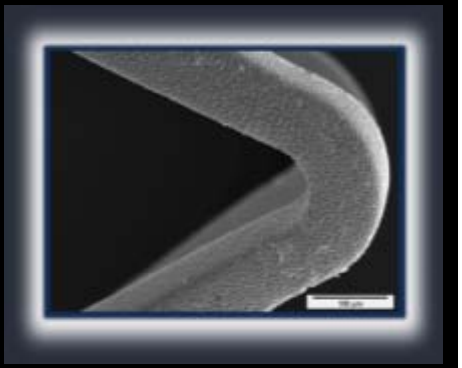
§ Polymer free Paclitaxel.

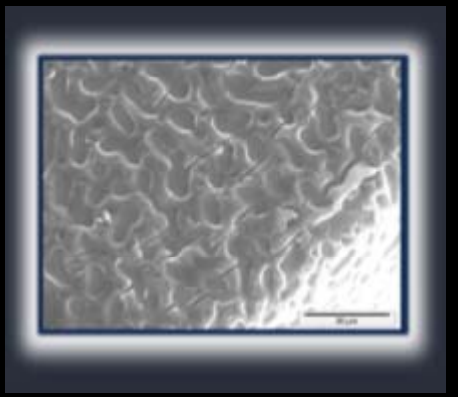
§ 2.5µg/mm² dose.

§ Boost-release (60% in 2 days)

§ Profile release established in 30 days (98% of the drug)

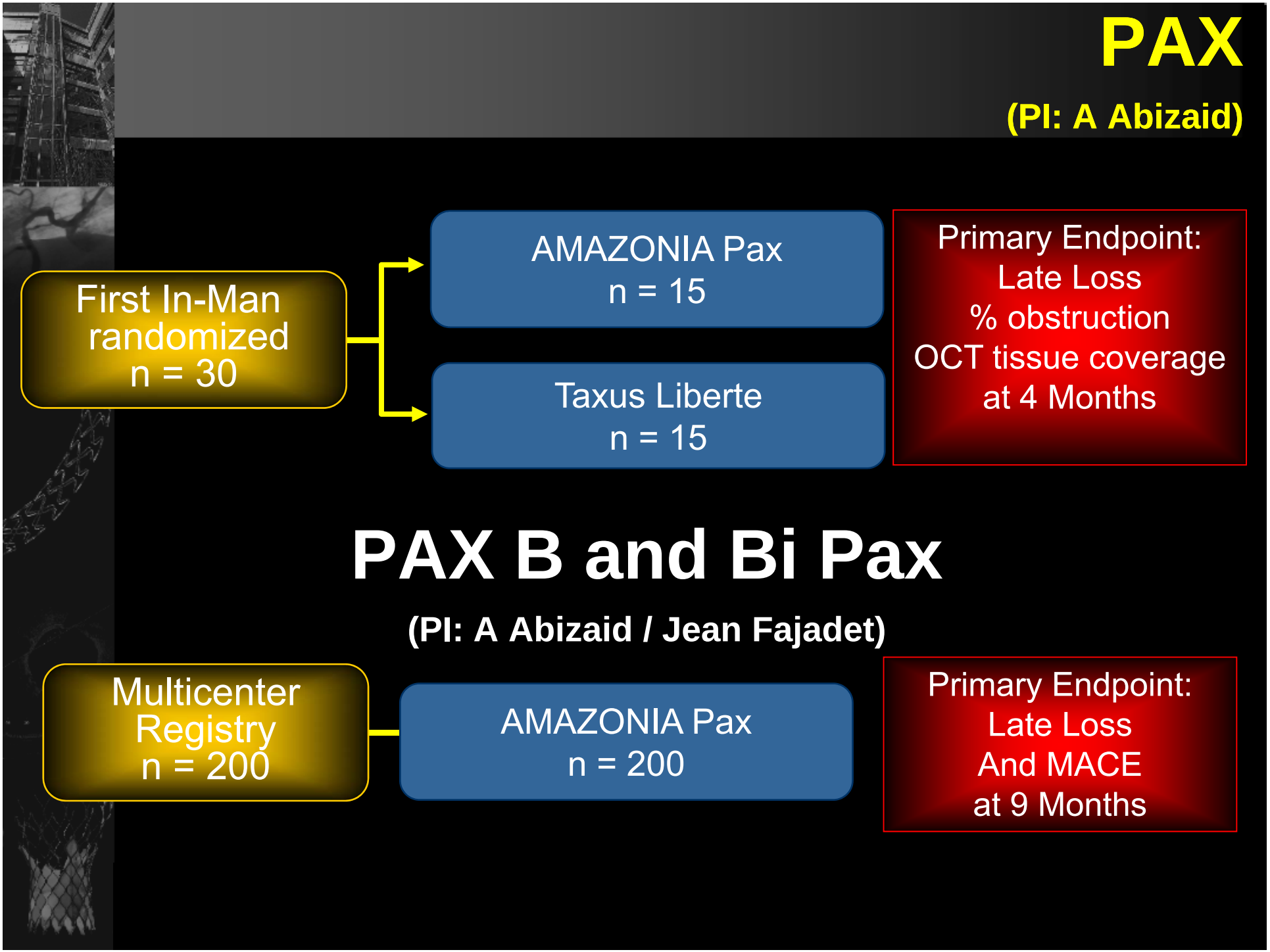
§ Back to regular Chromium Cobalt after 45 days.





PAX

(PI: A Abizaid)



PAX B and Bi Pax

(PI: A Abizaid / Jean Fajadet)

VESTASYNC II
Polymer-Free Sirolimus-Eluting Stent

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


DES without polymer but optimal release kinetics are the future since this eliminates one additional foreign body which has the potential to cause negative interactions

Thank you