Angioplasty Summit 2005
Seoul, Korea

New Drug-Eluting Stents

Alex Abizaid, MD, PhD
Instituto Dante Pazzanese de Cardiologia
Columbia University Medical Center

DANTE
PAZZANESE

New DES Systems

- Estradiol-Eluting Stent
- Biolimus A9-Eluting Stent
- Paclitaxel-Eluting Conor Stent
- ZoMaxx ABT 578-Eluting Stent
- Pimecrolimus-Eluting Avantec Stent

New DES Systems

- Estradiol-Eluting Stent
- Biolimus A9-Eluting Stent
- Paclitaxel-Eluting Conor Stent
- ZoMaxx ABT 578-Eluting Stent
- Pimecrolimus-Eluting Avantec Stent

17β-Estradiol: Restenosis

"Vasculoprotective"

- ↓ "response to injury" / ↑ vascular healing
  - ↑ re-endothelialization
  - ↓ intimal proliferation and migration
  - ↓ adventitial fibroblast cell migration

Histomorphometric Analysis

Control	Low dose 17 β-estradiol	High dose 17 β-estradiol

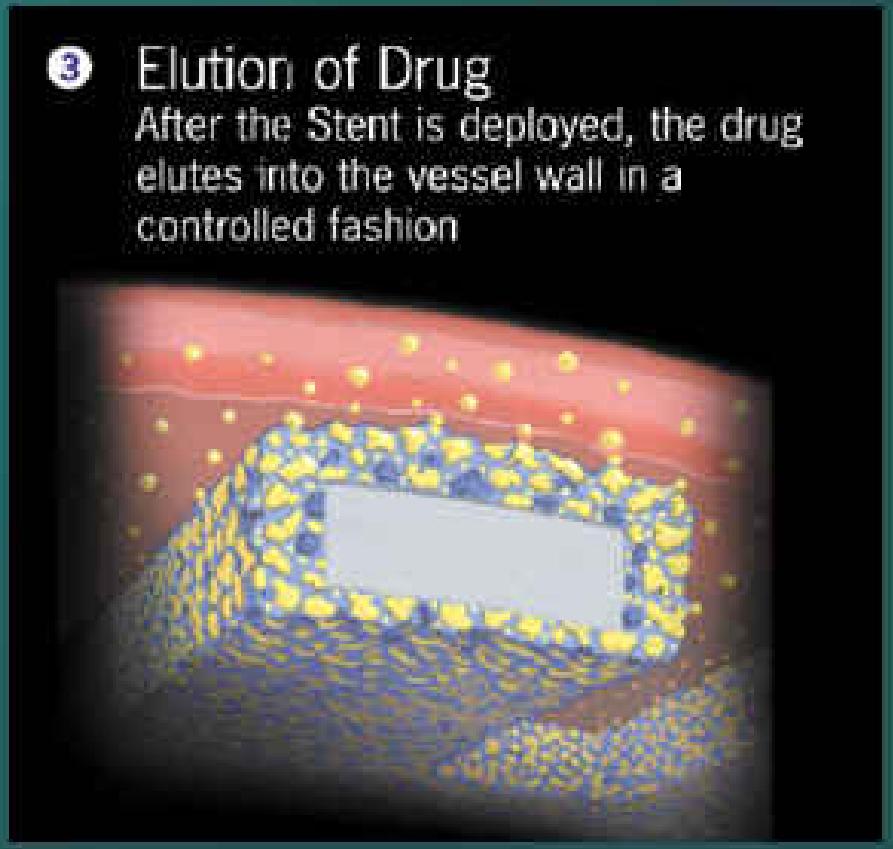
40% reduction in intimal area for high vs. control stents

New G., Moses J., Leon M. et al Circulation 2002 (abstract)

Stent-Based Drug Delivery

Biodivysio® Matrix LO stent

- PC polymer
- Double thickness
- 2.54 μg/mm^2 of 17β-estradiol



EASTER

Demographics

	n = 30
Mean Age (yrs)	61 ± 12
Male	70%
Prior MI	38%
Diabetes Mellitus	10%
Hypertension requiring meds	49%
Hypercholesterolemia requiring meds	27%
Current Smoker	31%

EASTER – QCA Results

In-stent

n = 30

	Post Intervention	6-month Follow-up
Reference (mm)	2.76 ± 0.56	
MLD (mm)	2.44 ± 0.52	1.89 ± 0.57
Diameter stenosis %	13.6 ± 10.4	28.2 ± 14.8
Late loss (mm)		0.54 ± 0.44
Binary restenosis		(2) 6.6%

Lesion length = 9.1 ± 2.4

EASTER – QCA Results

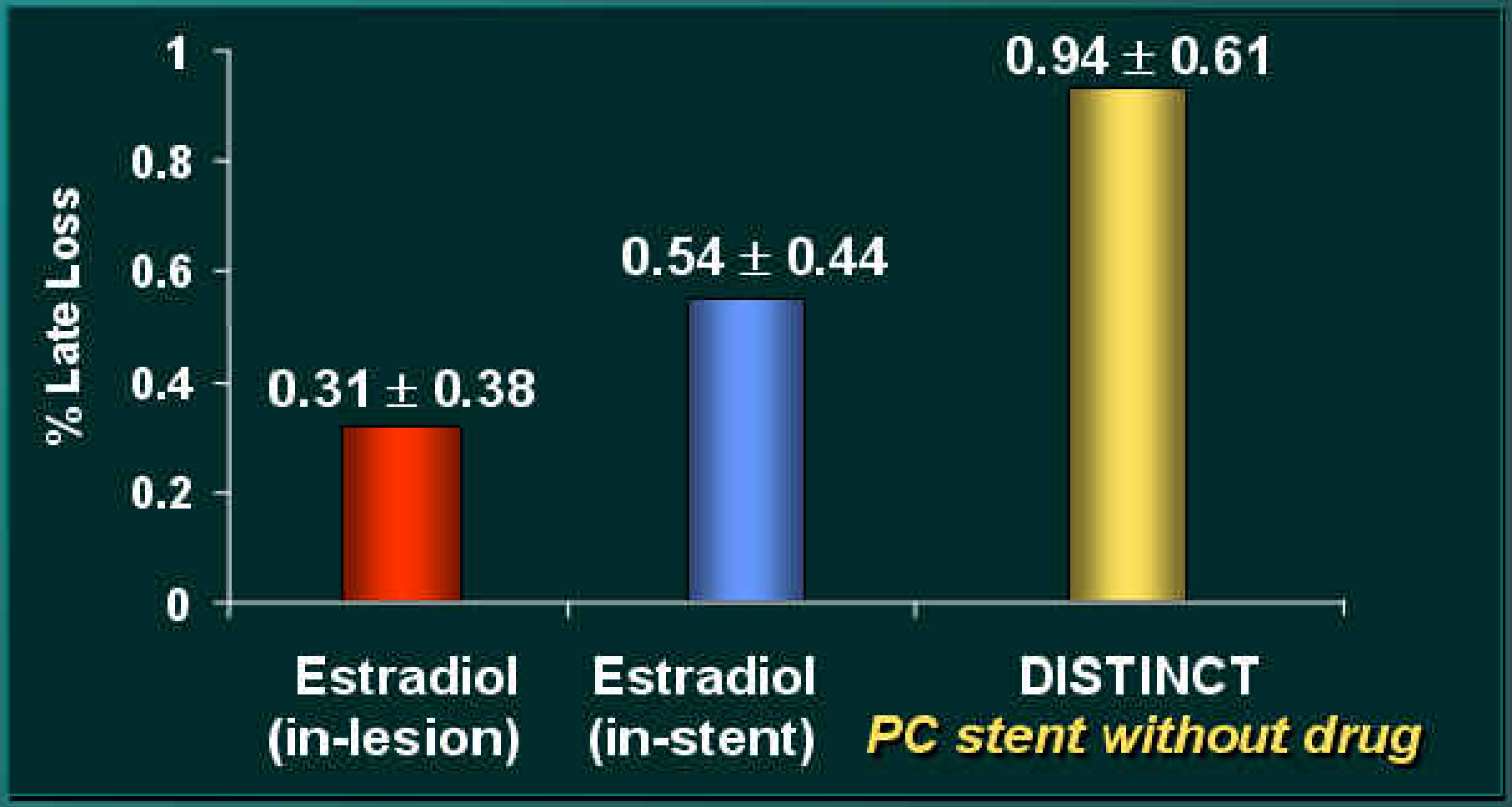
In-segment

n = 30

	Post Intervention	6-month Follow-up
MLD (mm)	2.04 ± 0.43	1.76 ± 0.56
Diameter stenosis %	23.4 ± 10.9	30.5 ± 14.9
Late loss (mm)		0.31 ± 0.38

BiodivYsio Trials

Late Loss Comparisons



EASTER – IVUS Results

In-stent

Vessel (mm^3)	268 ± 66
Stent (mm^3)	147 ± 43.6
Lumen (mm^3)	115 ± 41.9
Intimal hyperplasia (mm^3)	32.6 ± 14.7
% obstruction	23 ± 11%

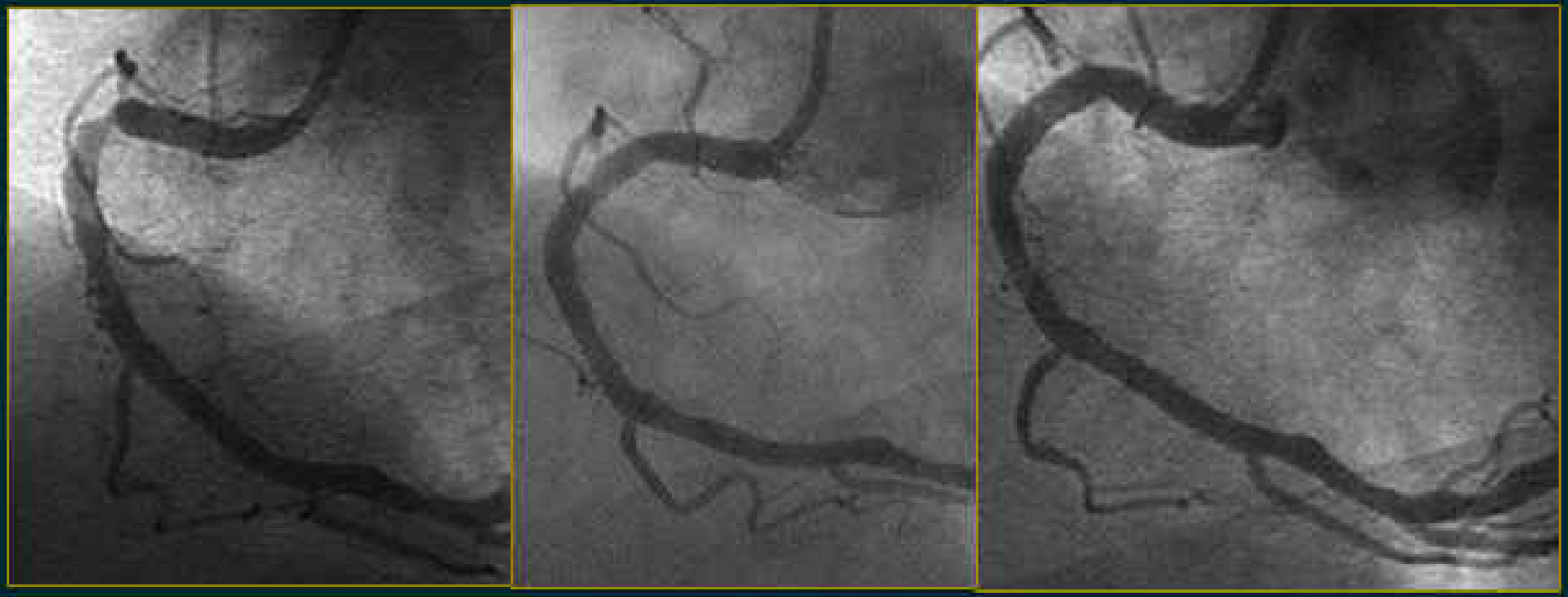
EASTER – Cumulative Clinical Follow-up

N=30	6 mos	1 year	2 years
Death (non-cardiac)	0%	3.3%	3.3%
Q wave MI	0%	0%	0%
TLR	3.3%	3.3%	3.3%
Non-TLR (other vessel)	3.3%	3.3%	3.3%
Event-free survival	93.4%	90.1%	90.1%

EASTER

17ß-Estradiol-Eluting Bio*divYsio* Stent

Pt: MMSN

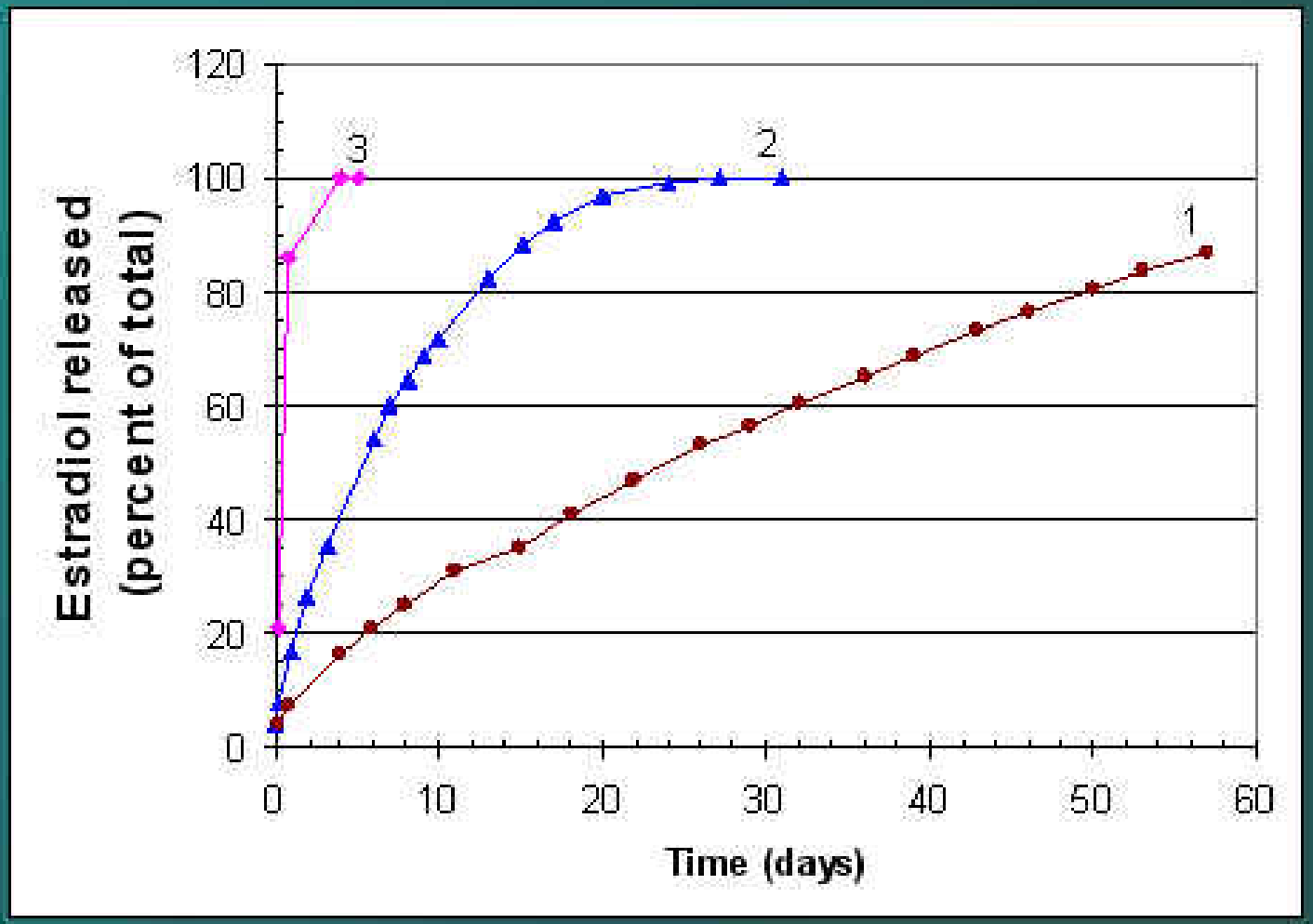


PRE | POST | FU 6 MONTHS

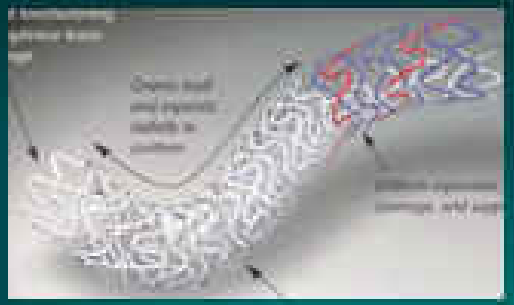
17β-Estradiol: Elution Kinetics from PC Coating

In-vitro release into large volume of PBS saline solution at 37°C

17β-Estradiol: Elution Kinetics from Durable Biostable Polymer



17β-Estradiol: The Future



R Stent (open cell, flexible, good scaffolding

17β Estradiol

Estradiol Eluting Stent

Biostable polymer (PEVA + PBMA)

ETHOS I: Study Design

Inclusion Criteria:
single lesion
2.5-3.5 mm ref diam
≤20 mm length

90 Pts Randomization

Exclusion Criteria:
AMI
low EF
complex lesions

30 pts R-stent

30 pts Ethos
Fast release

30 pts Ethos
Slow release

Endpoints:

Primary: ***IVUS % volume obstruction***
MACE

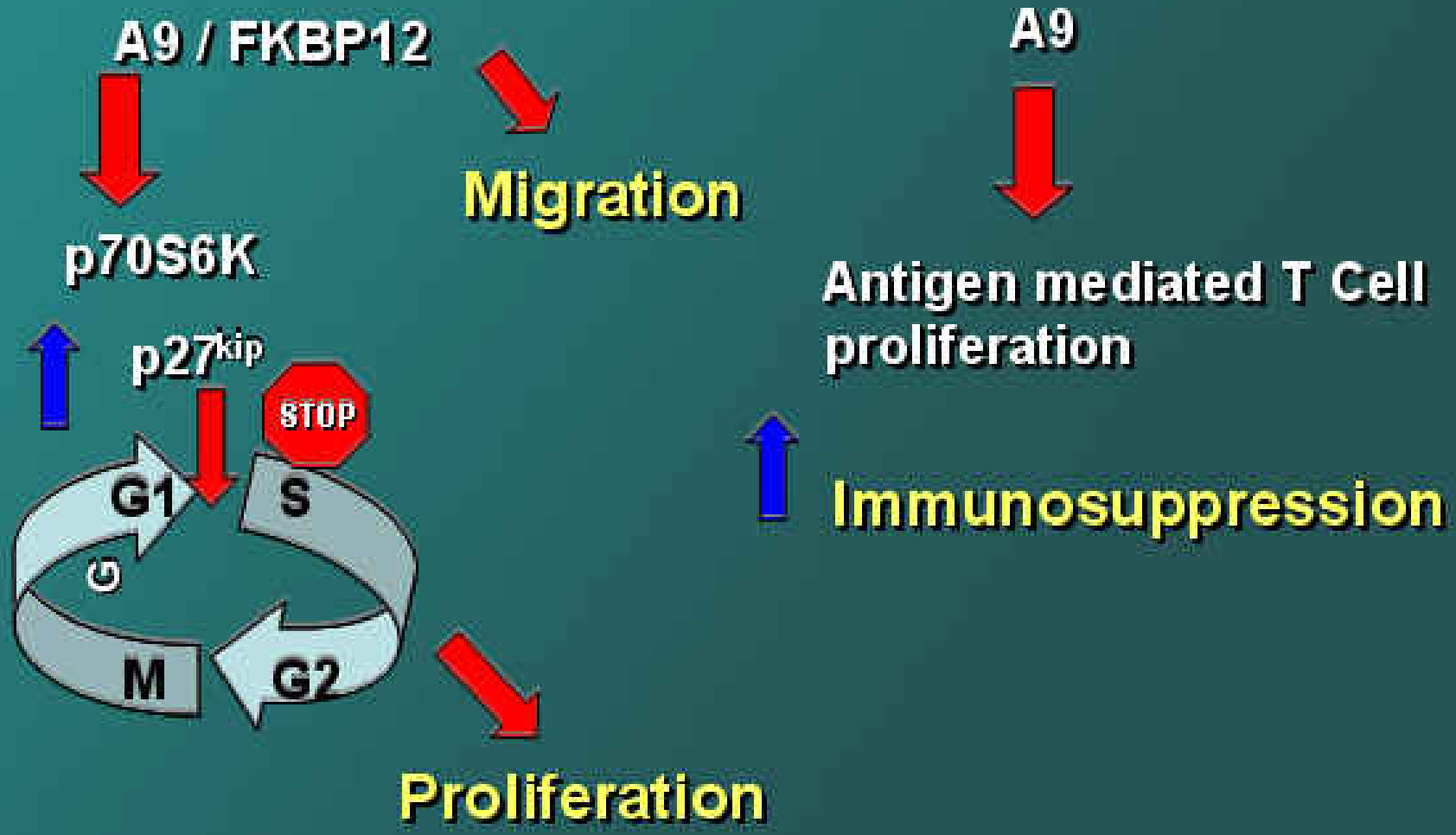
Secondary:
Angio - late loss, %DS, BR (in-stent and in-lesion)
IVUS - Intimal volume
Clinical – ST, TLR, TVF

6 mos angio/IVUS FU
1,6,12 mos clinical FU

New DES Systems

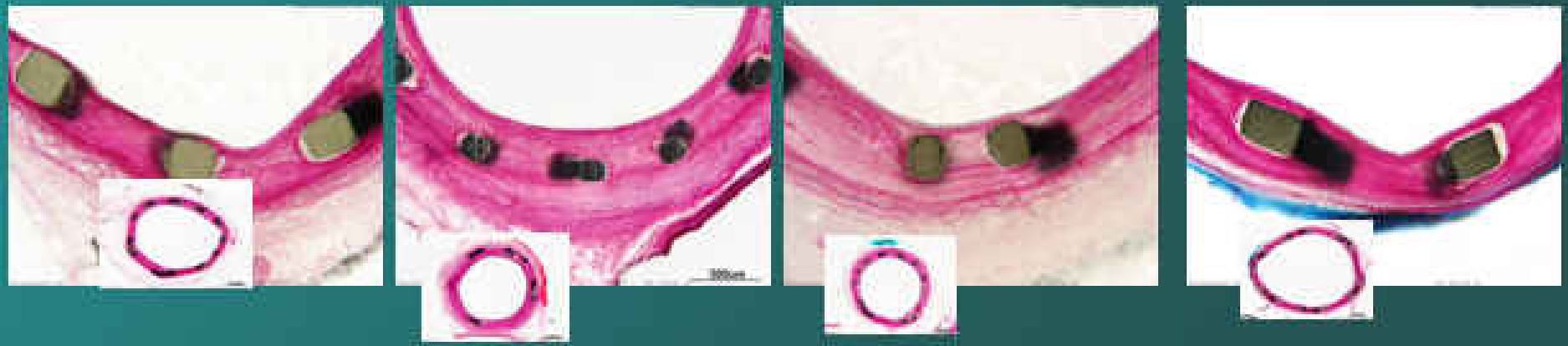
- Estradiol-Eluting Stent
- Biolimus A9-Eluting Stent
- Paclitaxel-Eluting Conor Stent
- ZoMaxx ABT 578-Eluting Stent
- Pimecrolimus-Eluting Avantec Stent

Proposed Mechanism of Action of Biolimus A9

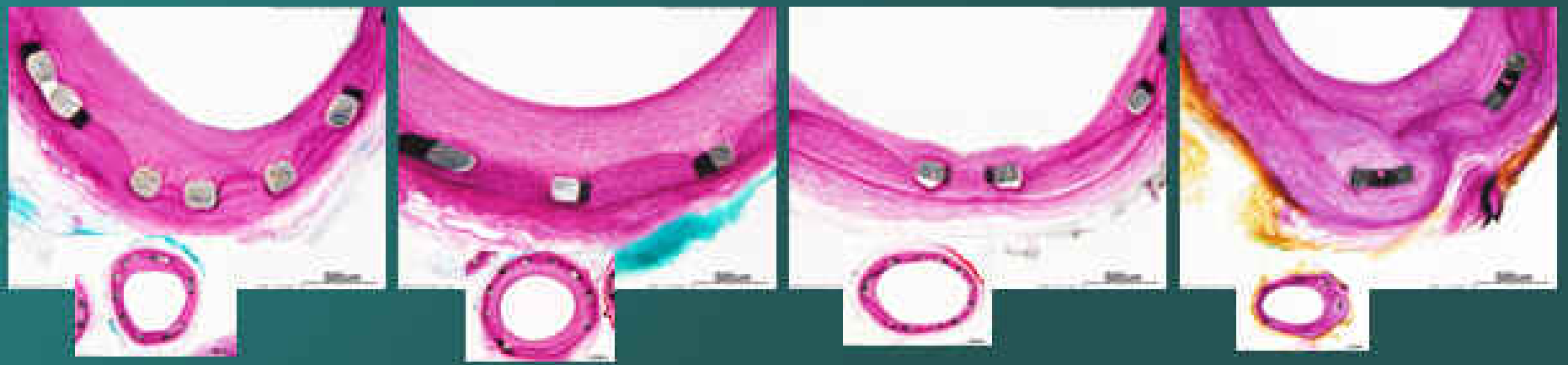


28 Day Implants

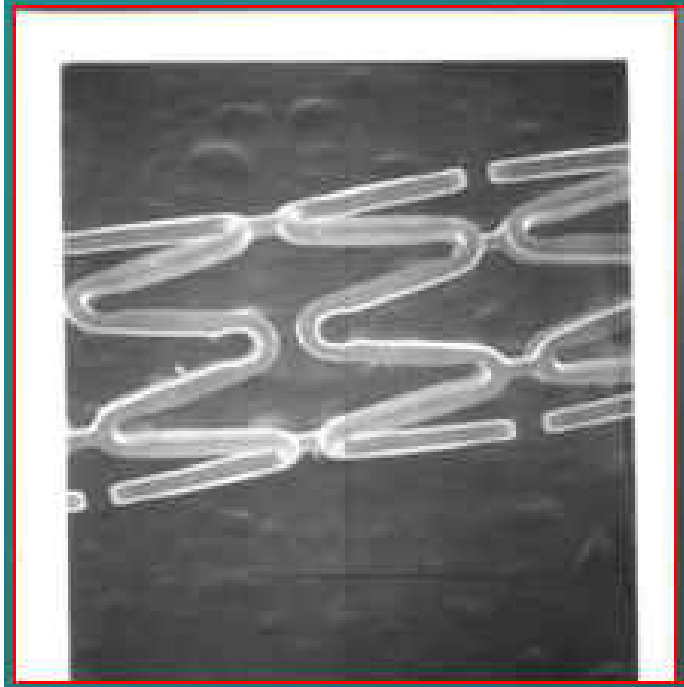
PLA/Biolimus A9™ coating vs. control in 20% swine overstretch model



S-STENT bare control

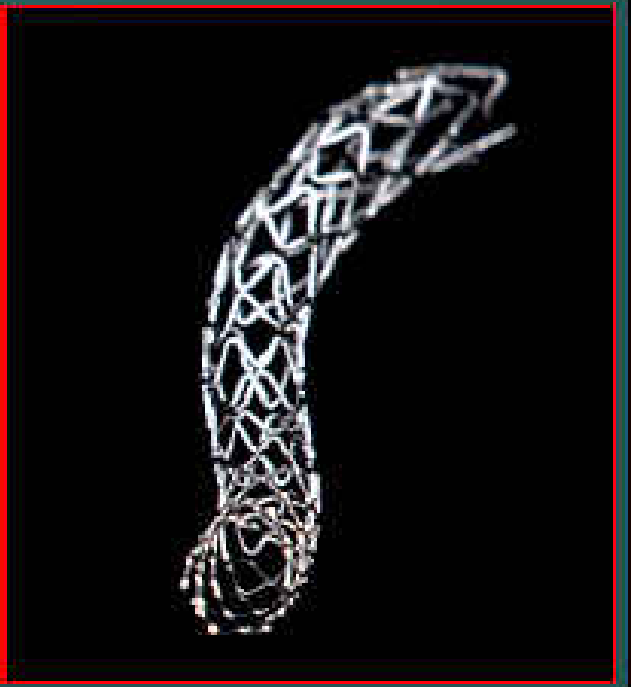


S-Stent™ Features



Corrugated ring Design

Quadrature-link Structure



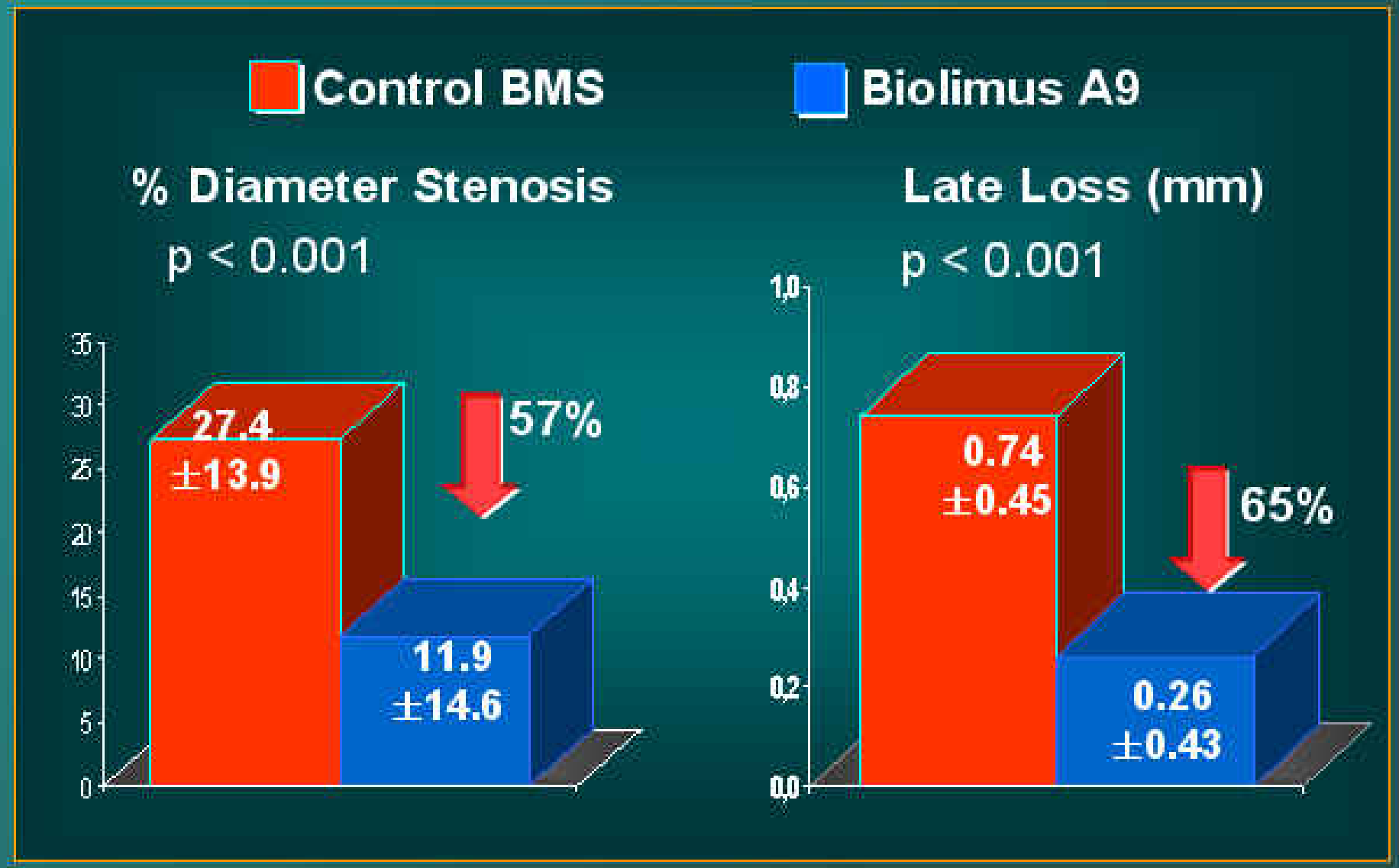
Serpentine Design

STEALTH Study Design

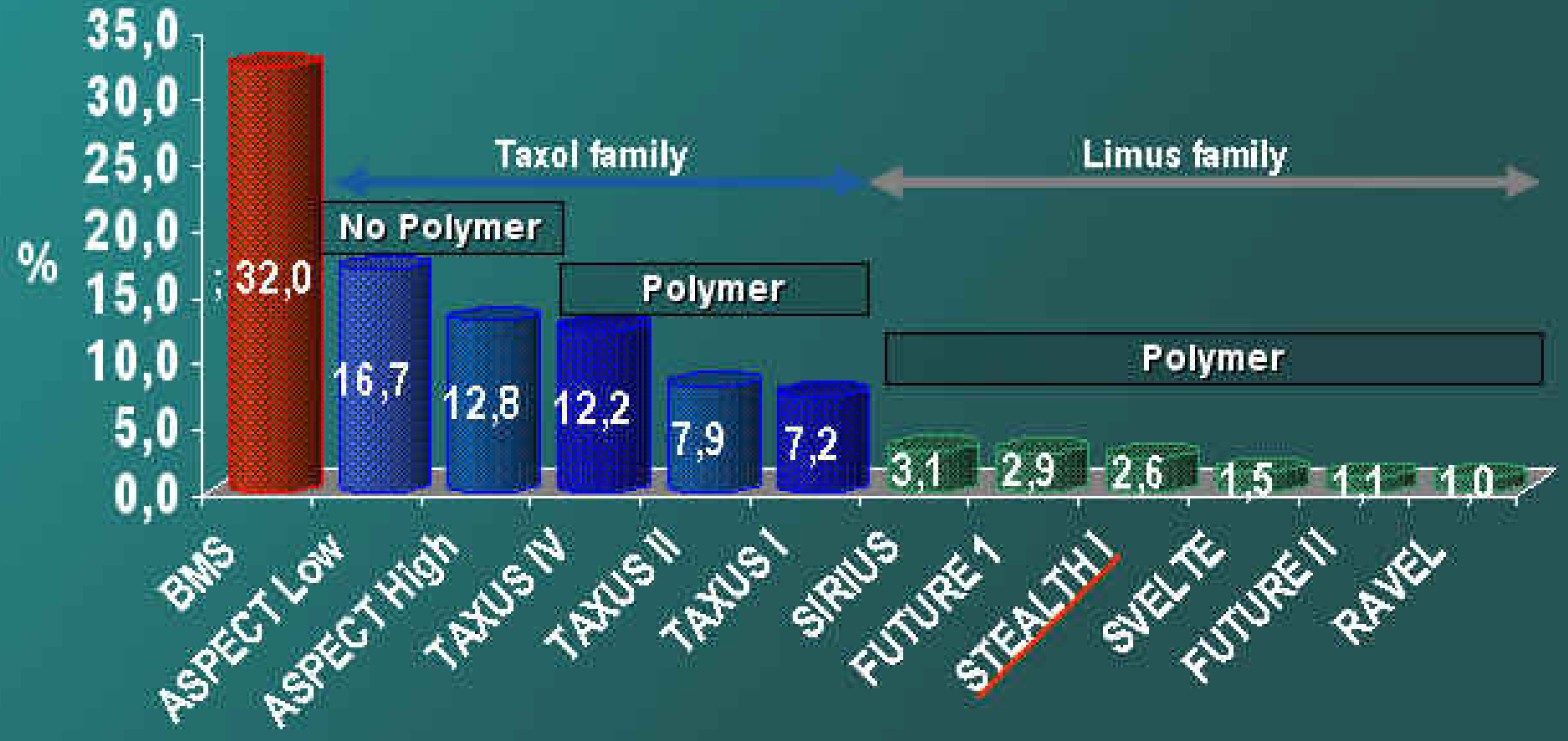
PI: Eberhard Grube

STent Eluting A9 BioLimus Trial in Humans

In-Stent Angiographic Results-6 Months

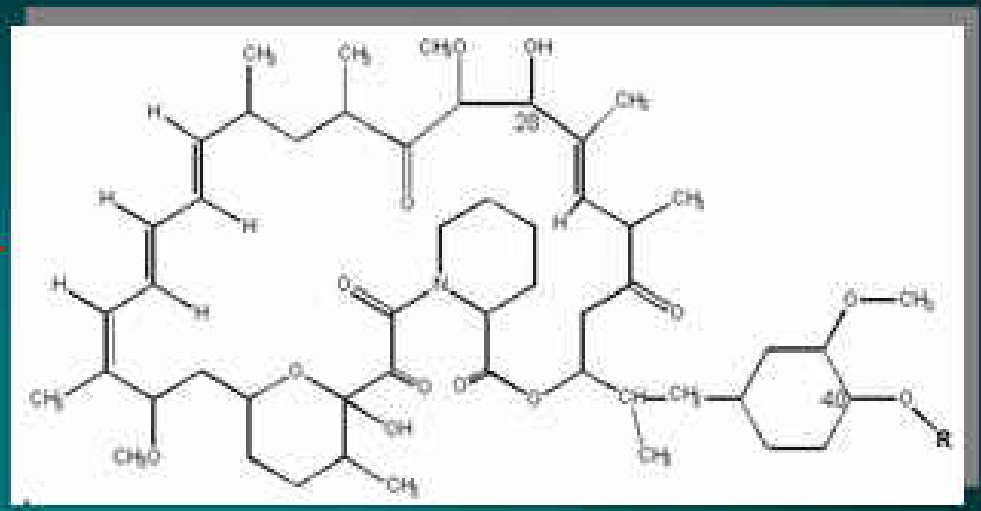


Comparison of Neointimal Volume



AXXESS PLUS™ System (Devax)

+



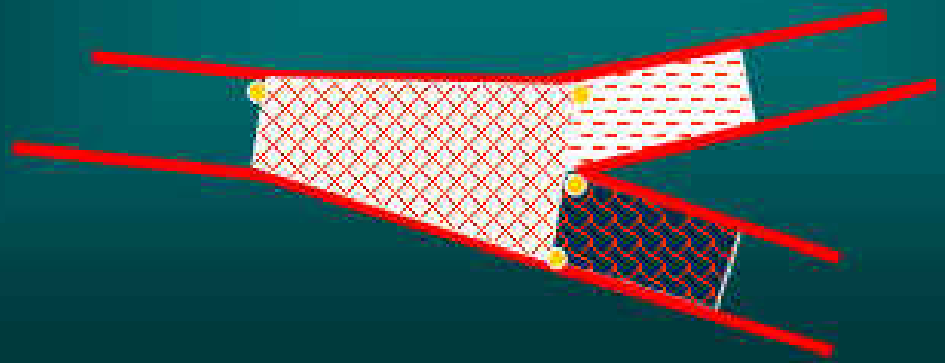
AXXESS
Stent

PLUS

Biolimus-A9
Anti-proliferative &
Bioerodable Polymer

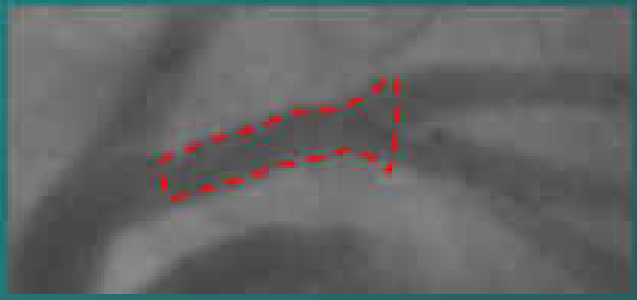
AXXESS PLUS Concept

- The Axxess Plus stent is implanted at the level of the carina.
- A successful implant will span the ostia of both branching vessels, indicated by the presence of one marker in each branch vessel.

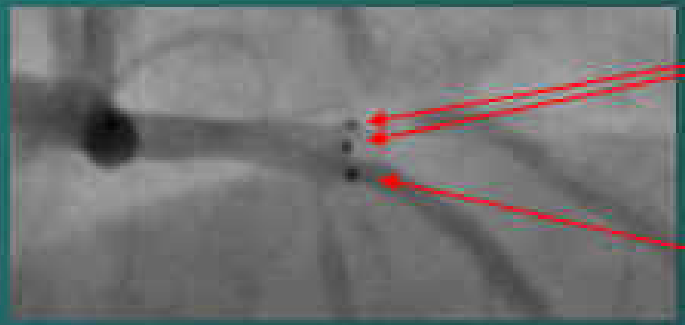


Why Self Expanding Stent?

The flared shape of the AXXESS PLUS stent matches the flared geometry of a bifurcation:

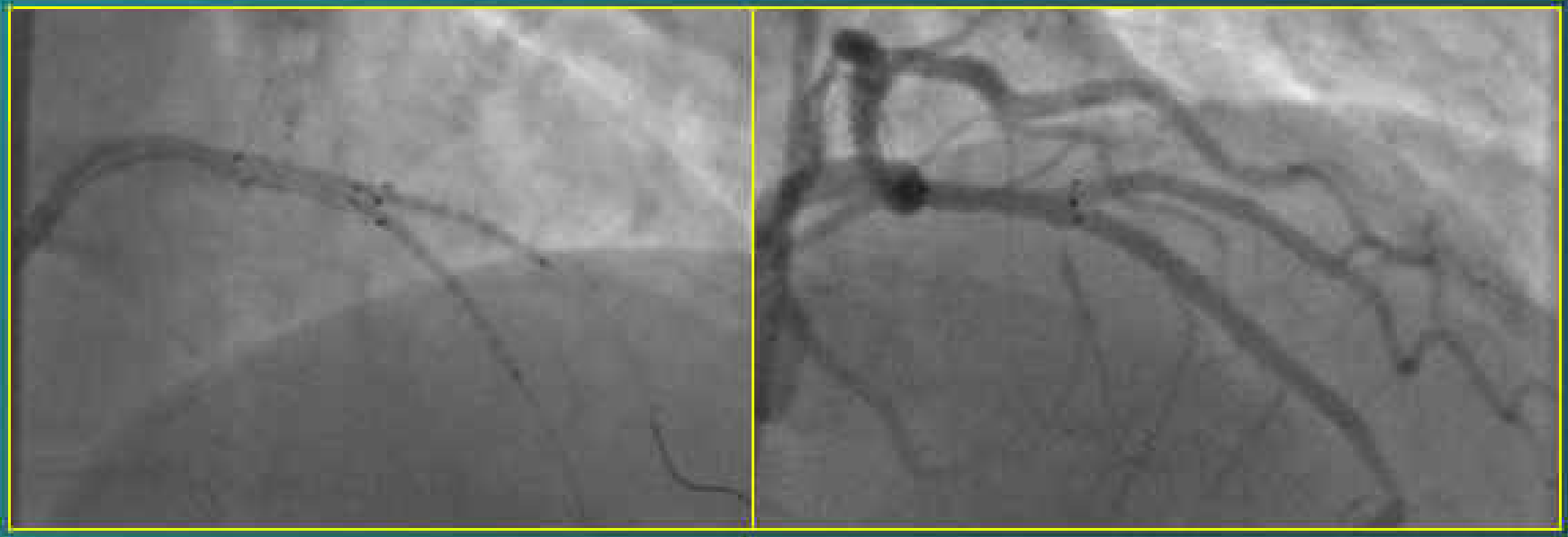


The Axxess Plus stent can expand into both the MB and SB, providing complete vessel coverage at the level of the carina:



Why Self Expanding Stent?

With the Axxess Stent covering the ostia, branch vessel stents are placed just distal to the bifurcation.



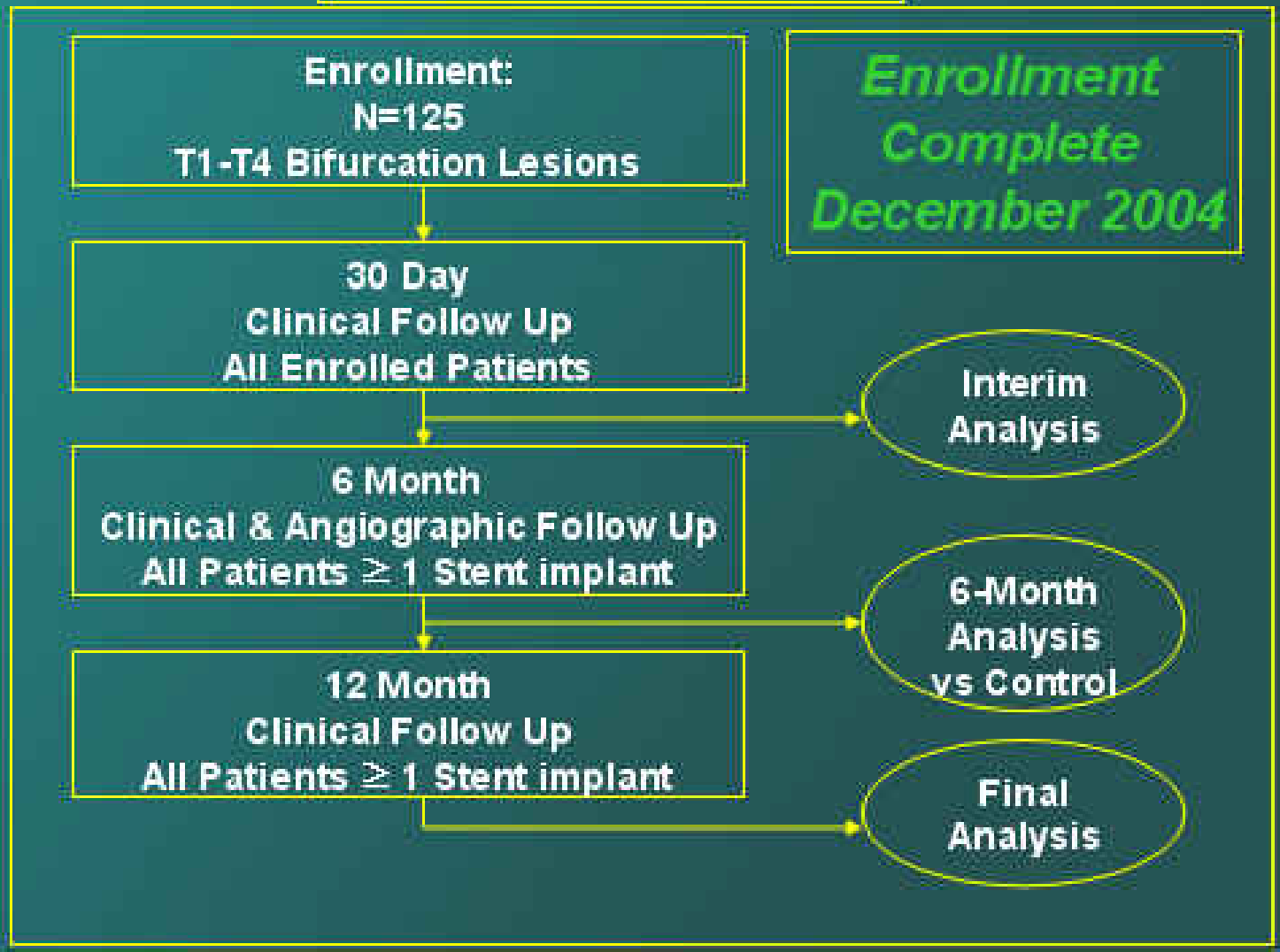
Distal stents are implanted in their natural shape, and do not need to be "remodeled" by PTCA to fit the anatomy of the bifurcation.

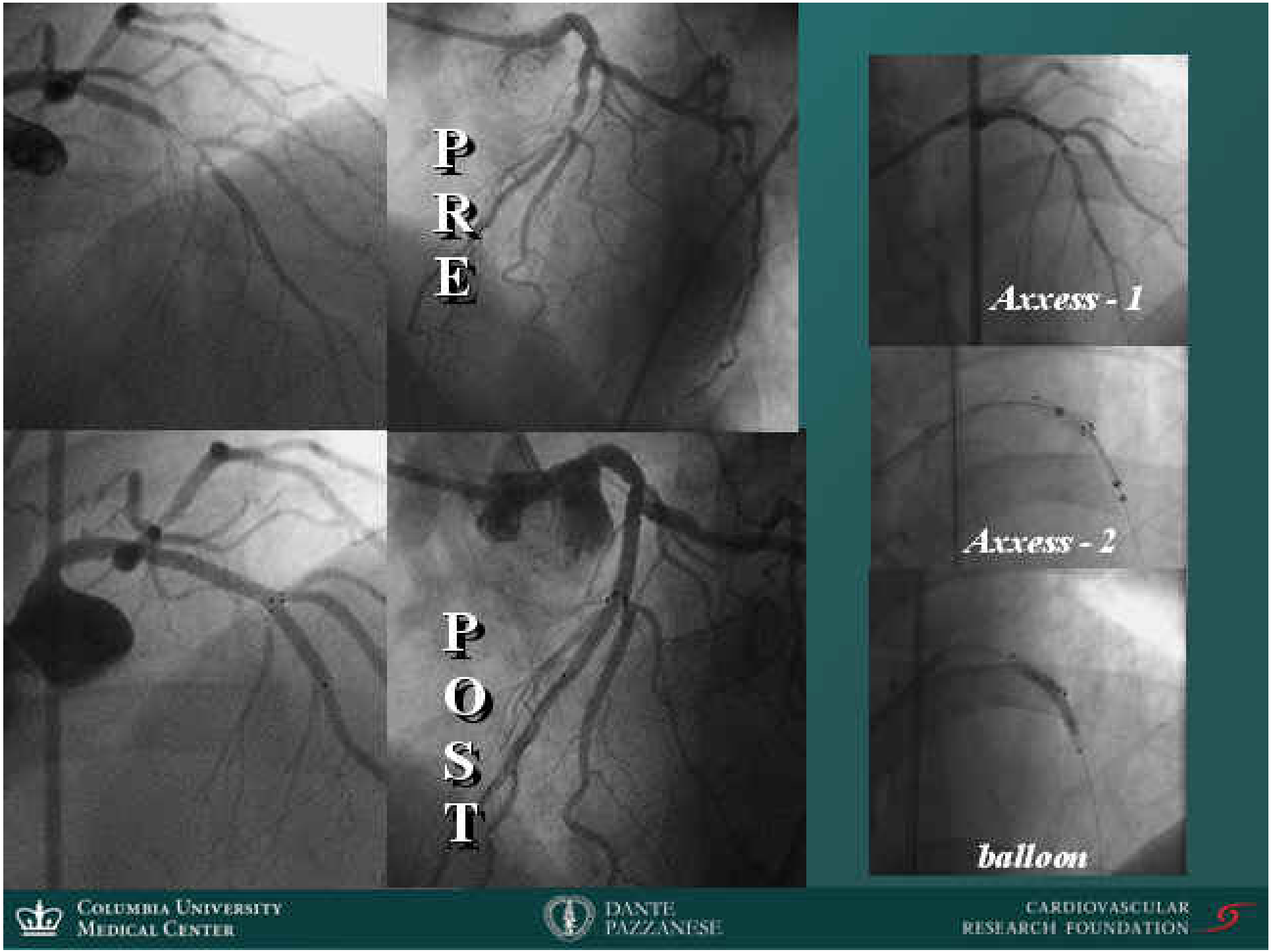
Study Design

Final results: TCT 2005

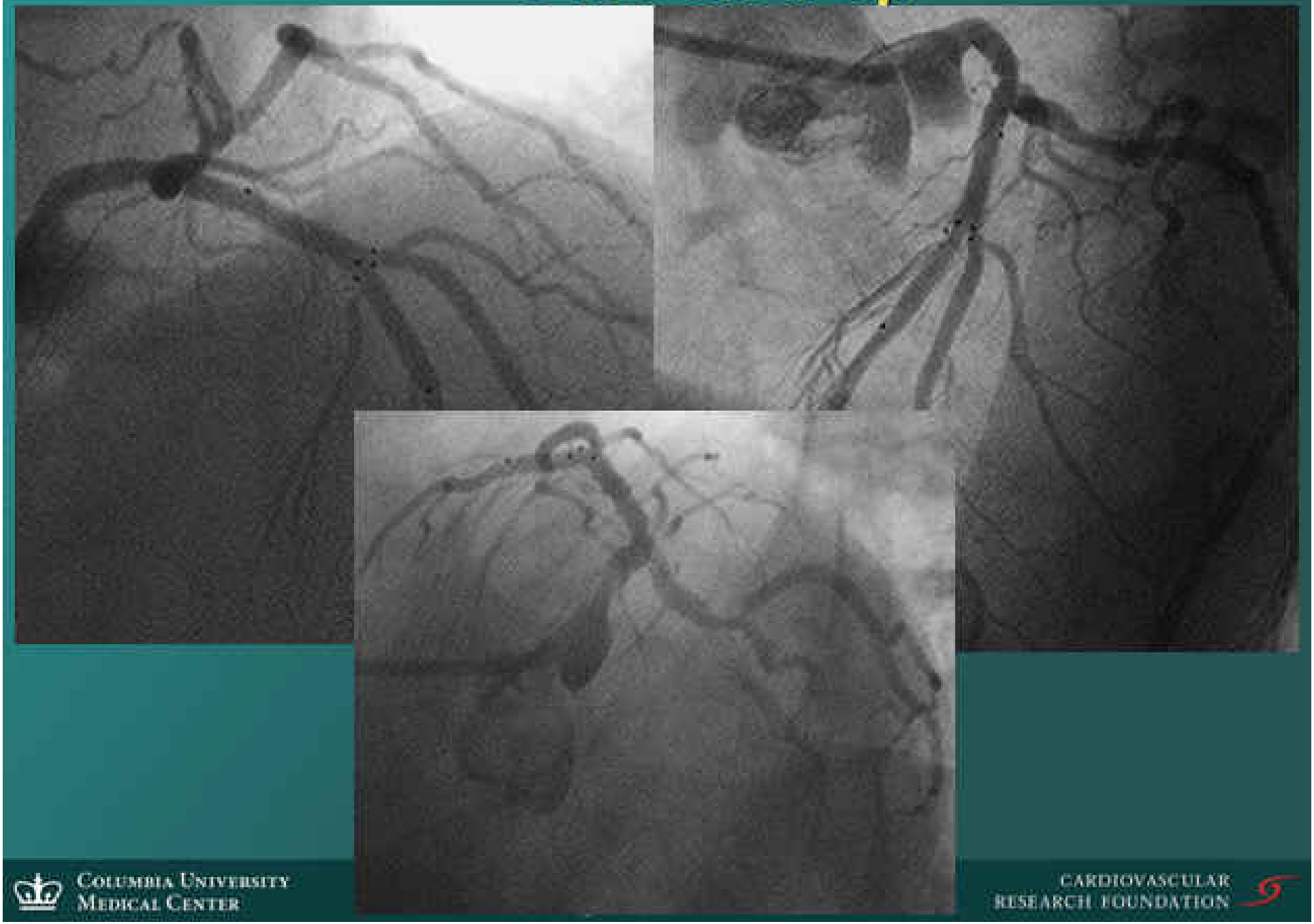
PI: E. Grube
Co PI: A. Abizaid

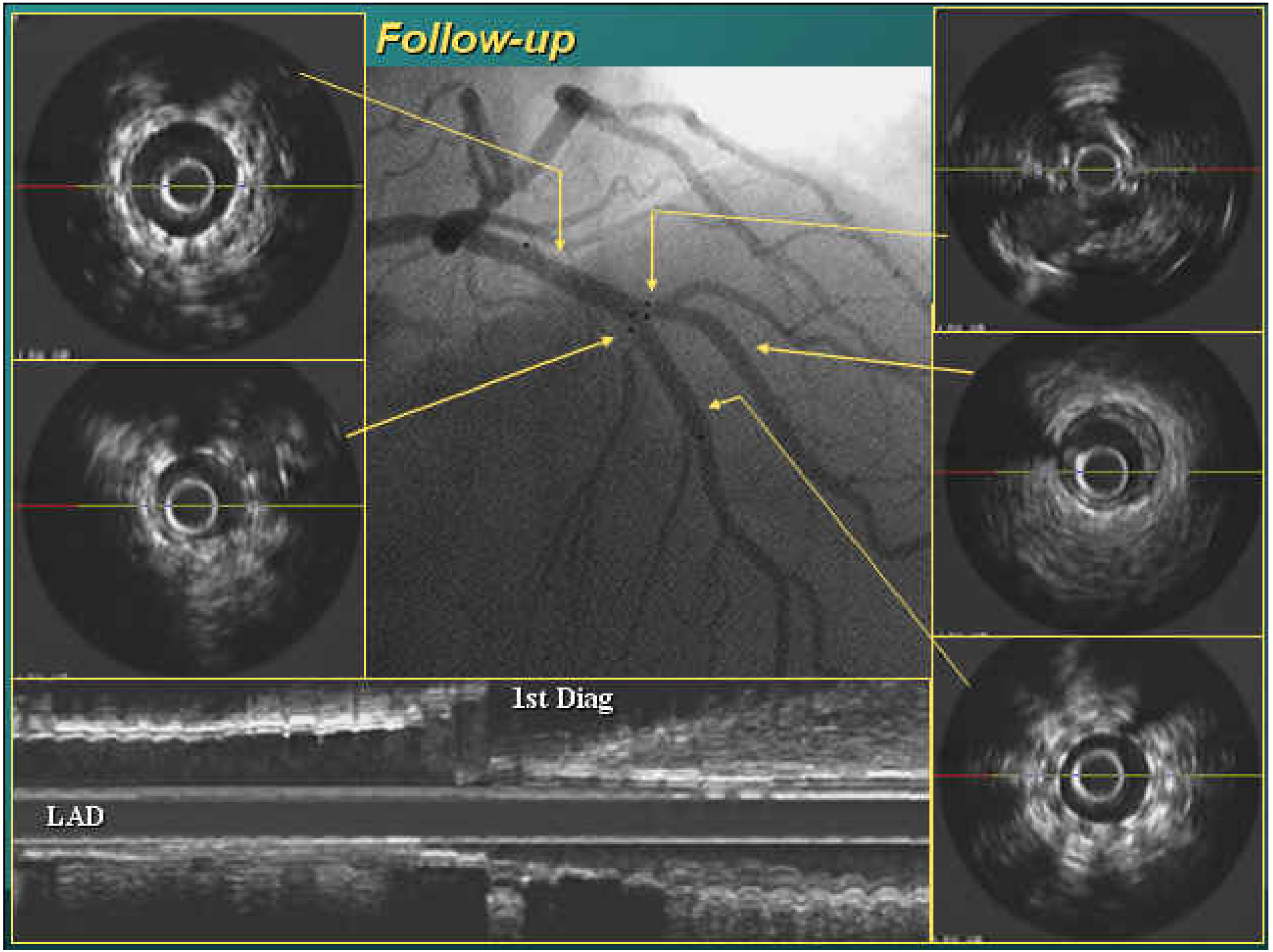
Axxess Plus Trial



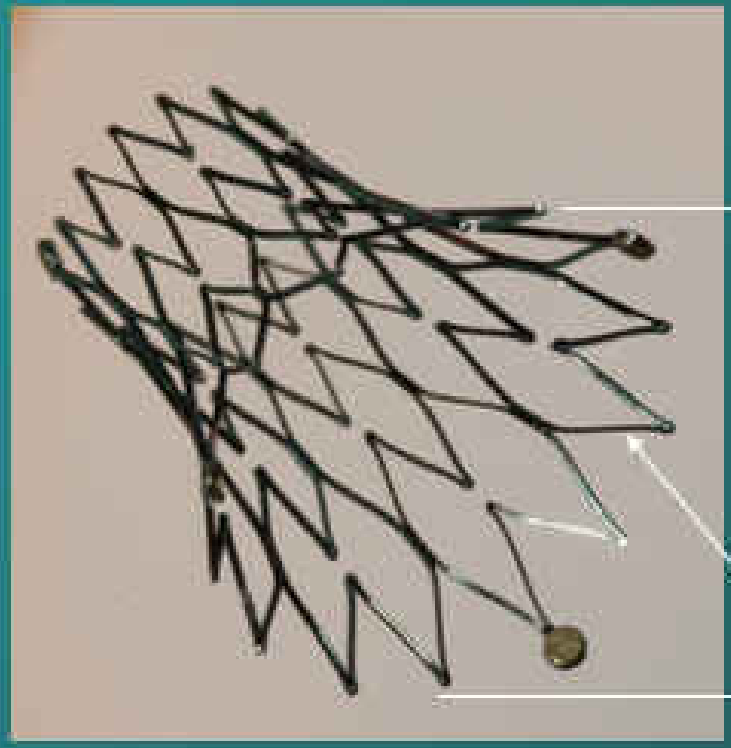

PRE
POST
Axxess - 1
Axxess - 2
balloon
COLUMBIA UNIVERSITY
MEDICAL CENTER
DANTE
PAZZANESE
CARDIOVASCULAR
RESEARCH FOUNDATION

6-m Follow-up




Follow-up
1st Diag
LAD

AXXESS PLUS LM System

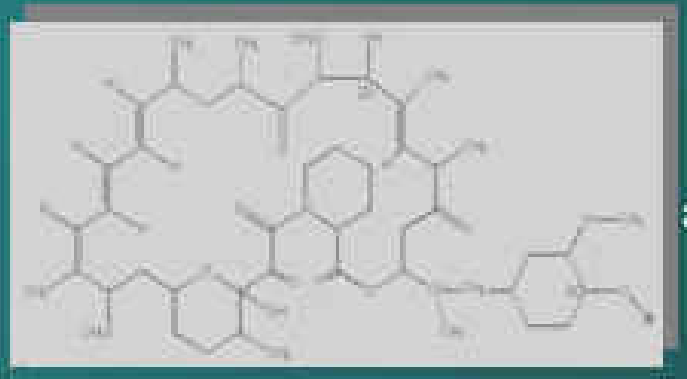


Flared Distal-End Stent Design

Self Expanding Nitinol Material

8, 10, or 12 mm
flare diameter

4.8F Rx Delivery System



Biolimus A9
antiproliferative
strut coating

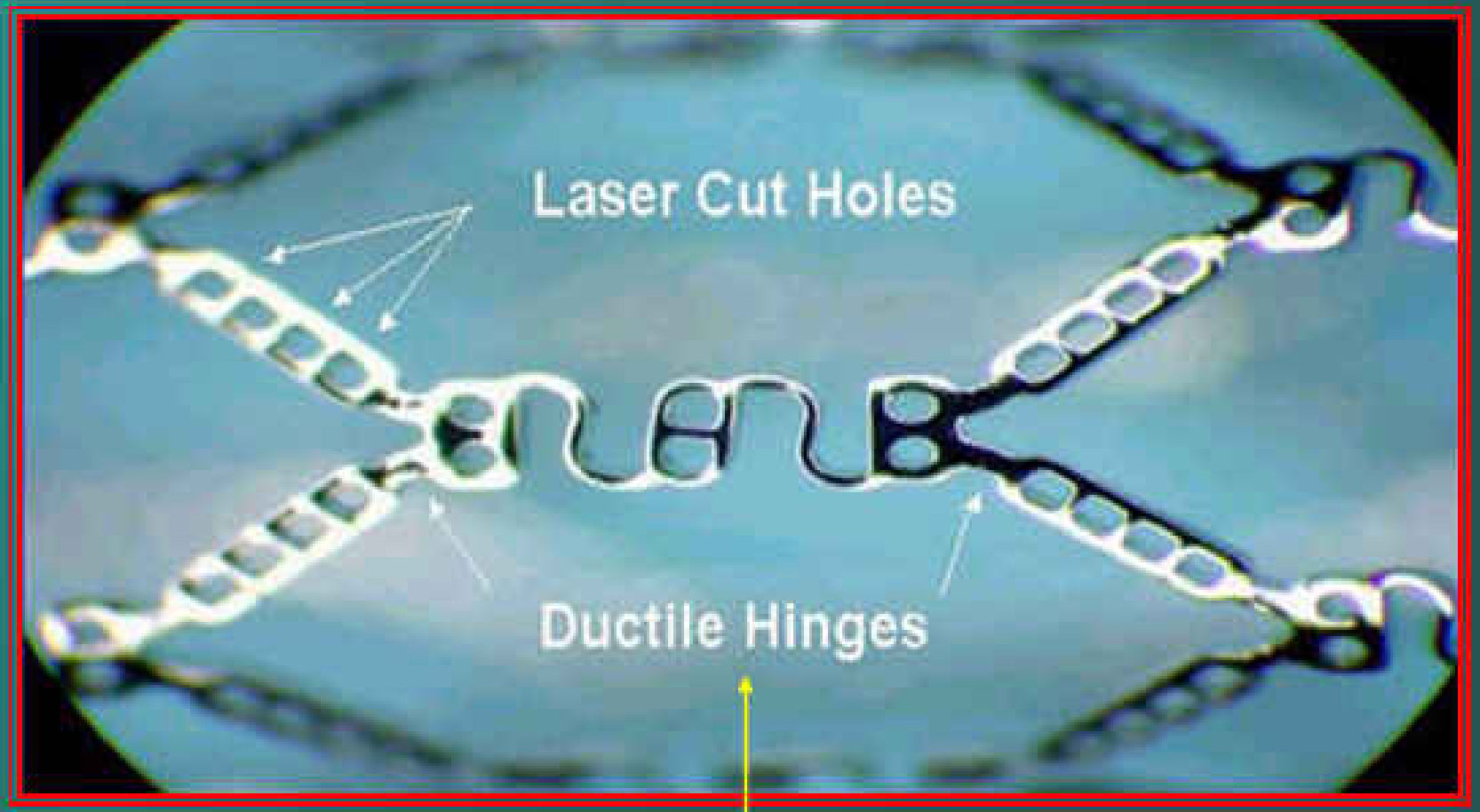
The AXXENT Trial

- **AXXENT**
  - Axxess Plus Biolimus Stent in LMCA Bifurcations Trial
- **Study Objective**
  - Evaluate the safety and efficacy potential of the Axxess Plus stent in LMCA bifurcation lesions (protected or not)
- **Study Design**
  - Multi-center registry, 40 patients; no concurrent control

New DES Systems

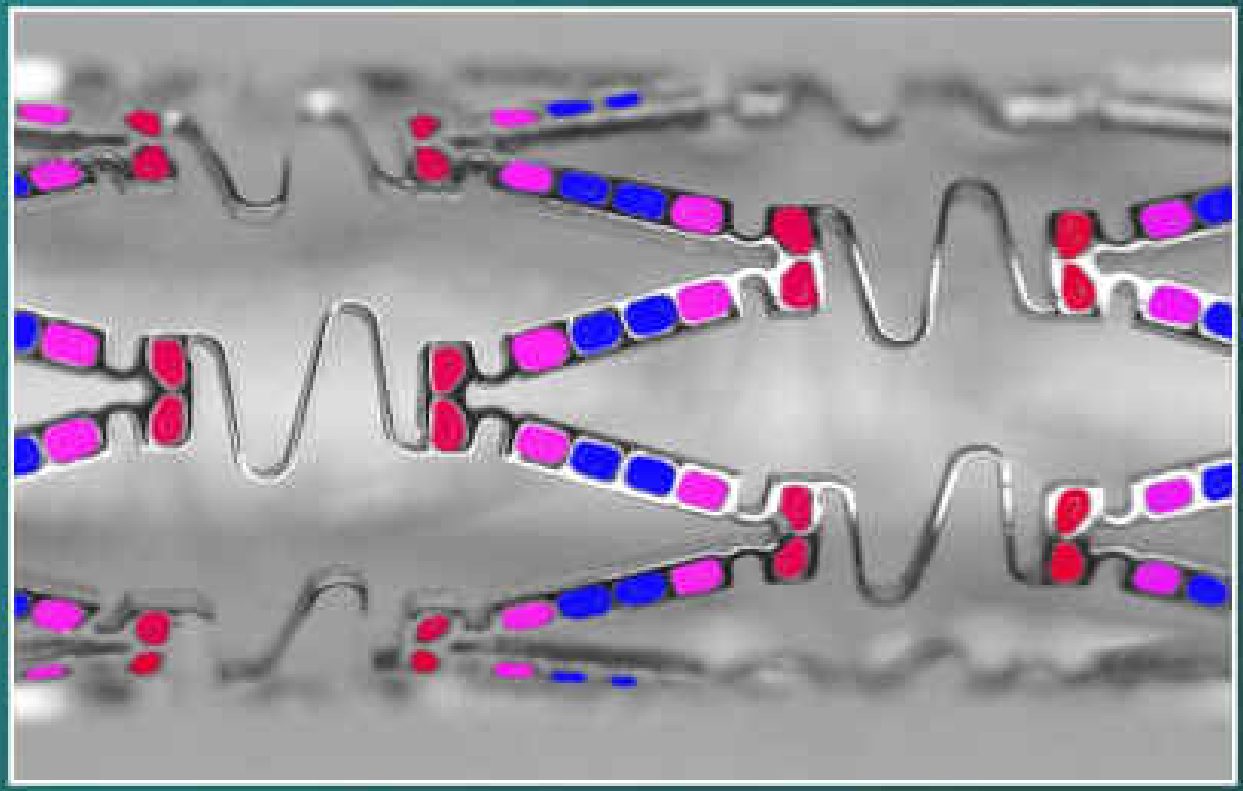
- Estradiol-Eluting Stent
- Biolimus A9-Eluting Stent
- Paclitaxel-Eluting Conor Stent
- ZoMaxx ABT 578-Eluting Stent
- Pimecrolimus-Eluting Avantec Stent

Technology : Conor Stent



Ductile Hinges allow struts to open without deformation

How Can Adequate Drug Dose Reach All Locations of the Vessel Wall?

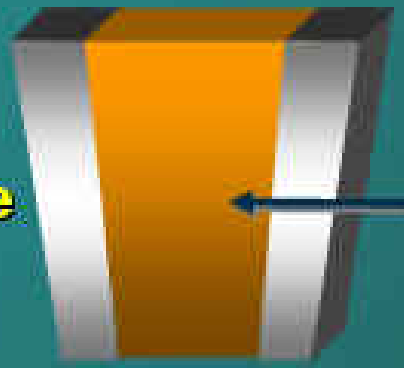


Polymer inlays are individually programmable for drug concentration enabling controlled spatial drug dose distribution.

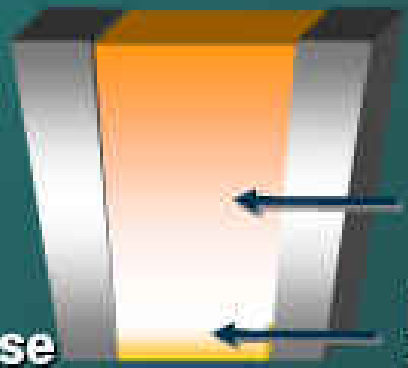
Conor Drug Release Technology

Mural Side

Single Drug Structure



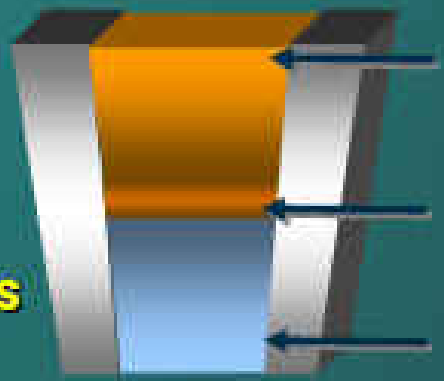
Simple Drug Reservoir Uniform Release



Drug Reservoir

Luminal Barrier Layer

Multiple Drug Structures



Drug A released to arterial wall

Barrier layer

Drug B released into bloodstream

Two Drugs, One Well

Two Drugs, Two Wells Two Directions

PISCES Trial

PI: P. Serruys

Paclitaxel In StentControlled Elution Study

Group 1	Group 2
0.10 µg/mm^2	0.10 µg/mm^2
5-6 Day	10 Day
(Bidirec.)	(Mural)
N = 30	N = 30

N=191 pts

- **Dose-Ranging Registry**
- **Single, *De Novo* Lesions**

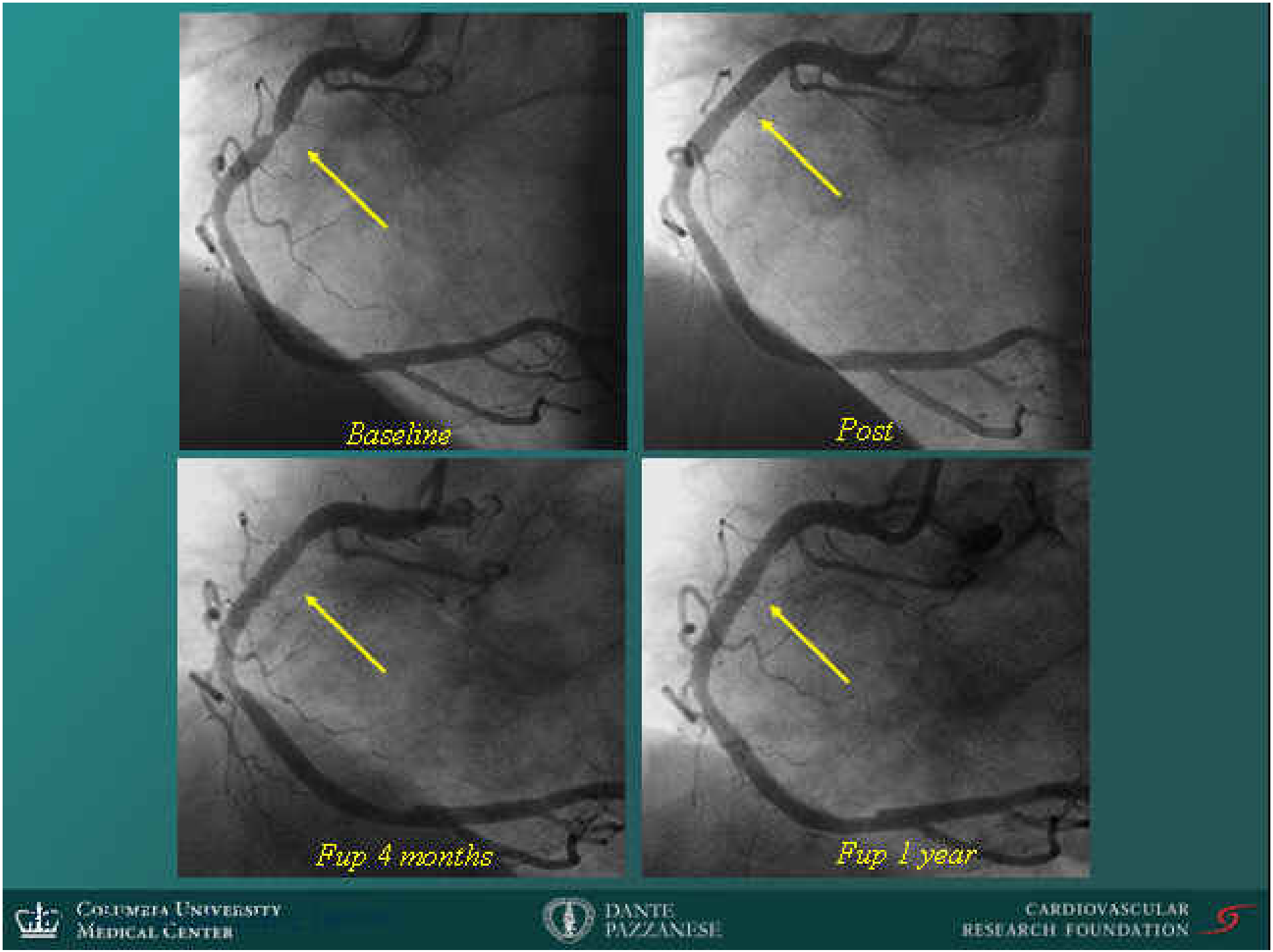
Group 3	Group 4
0.10 µg/mm^2	0.10 µg/mm^2
10 Day	30 Day
(Bidirec.)	(Mural)
N = 30	N = 30

Group 5	Group 6
0.30 µg/mm^2	0.30 µg/mm^2
30 Day	10 Day
(Mural.)	(Bidirec.)
N = 30	N = 30

4 & 12 Month Clinical and Angiographic Follow-up

QCA: In-stent analysis at 4 months

Unmatched pre-post-fup	D1 10µg 5d/b N=30	D2 10µg 10d/m N=30	D3 10µg 10d/b/0 N=31	D4 10µg 30d/m N=39	D5 30µg 30d/m N=30	D6 30µg 10d/b N=31
Lesion length (mm)	9.7	10.7	9.4	9.4	10.5	10.7
MLD (mm)						
post	2.60	2.70	2.57	2.68	2.52	2.49
fup	1.87	2.02	1.90	2.30	2.18	2.02
Late loss (mm)	0.72	0.67	0.70	0.38	0.37	0.48
Late loss index	0.49	0.38	0.46	0.22	0.25	0.32
Restenosis rate (%)	10.3	3.6	14.3	0.0	7.4	6.9


Baseline
Post
Fup 4 months
Fup 1 year
COLUMBIA UNIVERSITY MEDICAL CENTER
DANTE PAZZANESE
CARDIOVASCULAR RESEARCH FOUNDATION

EuroStar Trial

PI: K. Dawkins

CoStar Cobalt Chromium Paclitaxel-Eluting Stent

Registry 1
10 mcg
(30 days)
N = 145

Multicenter 2-arm Registry

Registry 2
30 mcg
(30 Days)
N = 150

Reported at ACC 2005:

- **Binary restenosis: 3.4%**
- **In-stent late loss: 0.26 mm**
- **In-segment late loss: 0.07 mm**
- **TLR: 1.7%**
- **MACE: 4.8%**

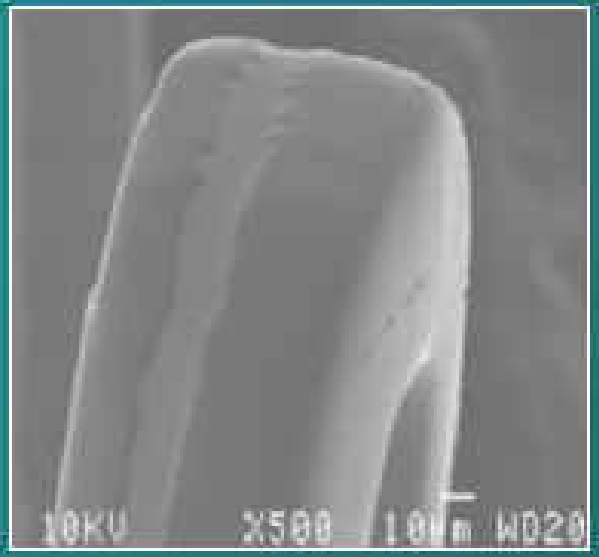
New DES Systems

- Estradiol-Eluting Stent
- Biolimus A9-Eluting Stent
- Paclitaxel-Eluting Cordis Stent
- ZoMaxx ABT 578-Eluting Stent
- Pimecrolimus-Eluting Avantec Stent

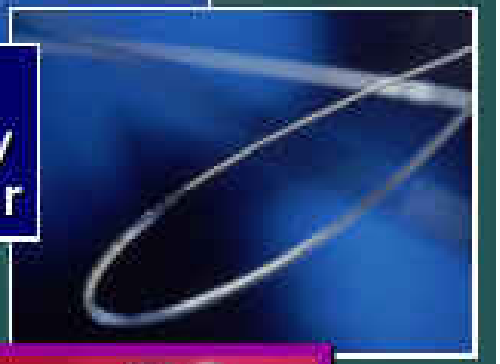
Abbott ZoMaxx Drug-eluting Stent

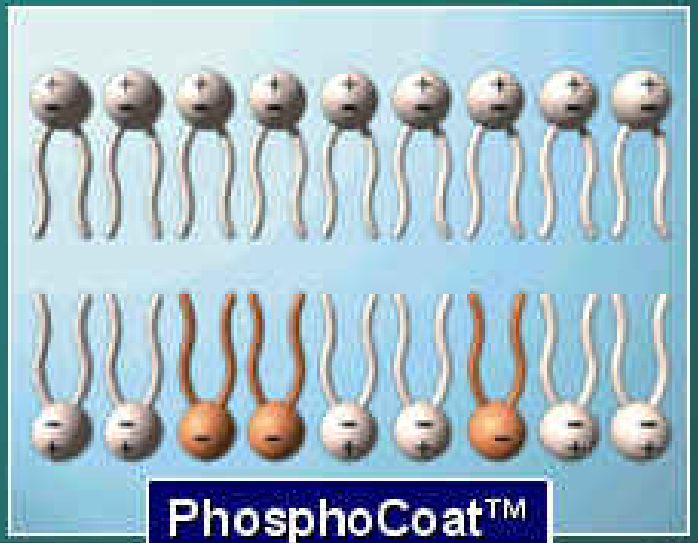
Triplex™ Material (SS, tantalum, SS)

A.R.C.™ Technology



Accel™ Delivery Catheter





PhosphoCoat™

Drug: ABT-578*

Final results:
TCT 2005

TriMaxx Trial

PI: Alex Abizaid

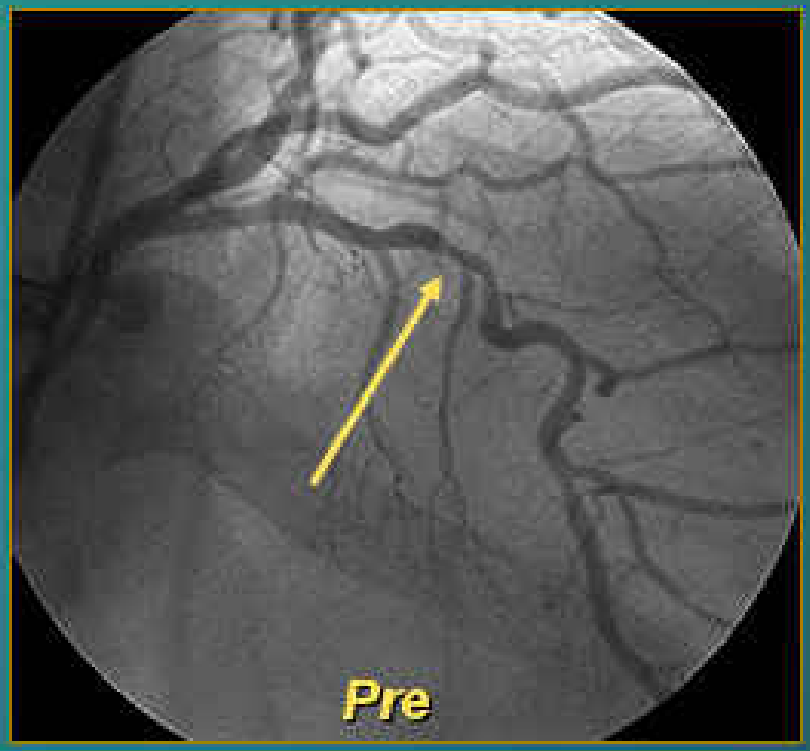
Single-vessel, *de novo* coronary lesions (Type A-B),
length ≥ 10 mm and ≤ 15 mm; RVD 3.0-3.75 mm

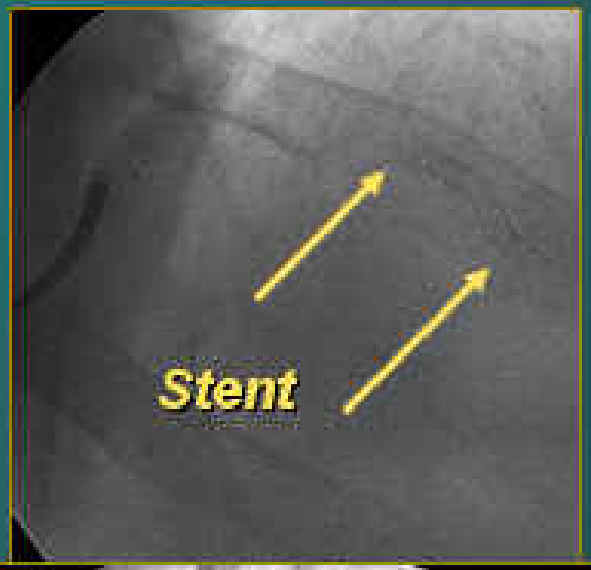
Stent Diameters	Stent Lengths
3.0 mm	18 mm
3.5 mm	18 mm

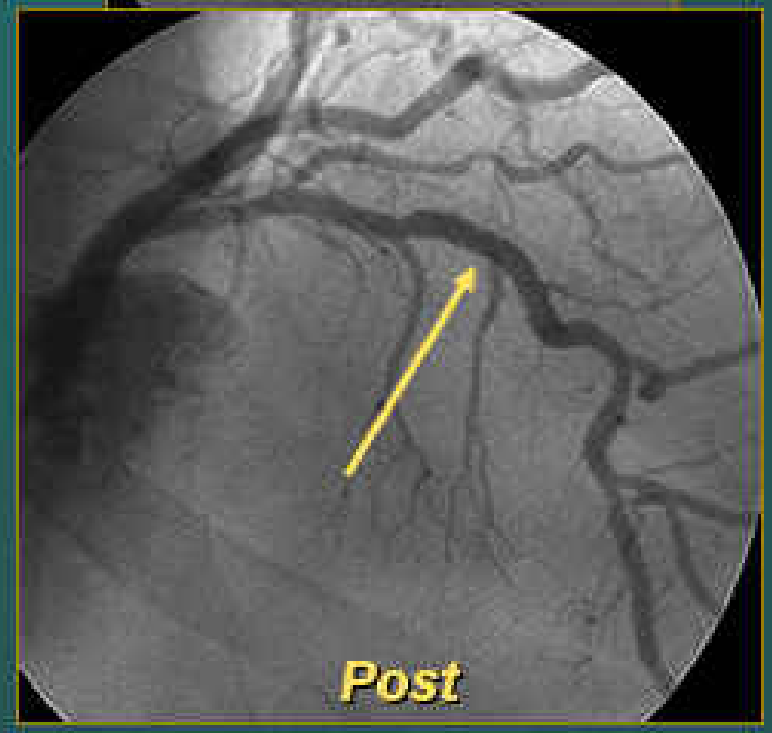
100 Subjects

Up to 5 Sites
– Brazil
- Germany

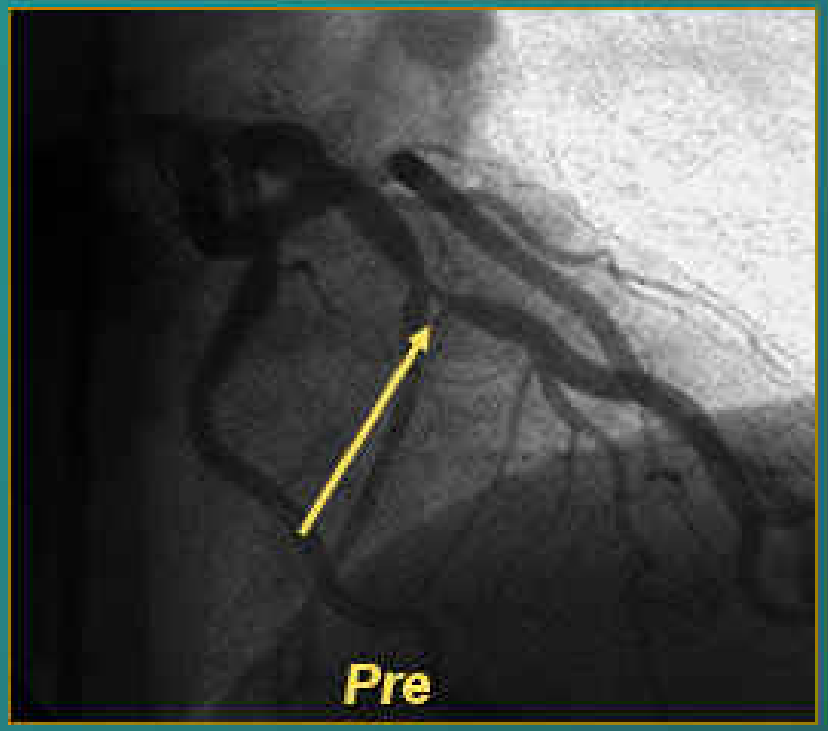
Primary Endpoint:	MACE at 30 days
Secondary Endpoints:	MACE, TLR, TVR, ABR, Late Loss at 6 months
Platelet Inhibition:	Clopidogrel/Ticlid (30 days), ASA 100 mg cont.

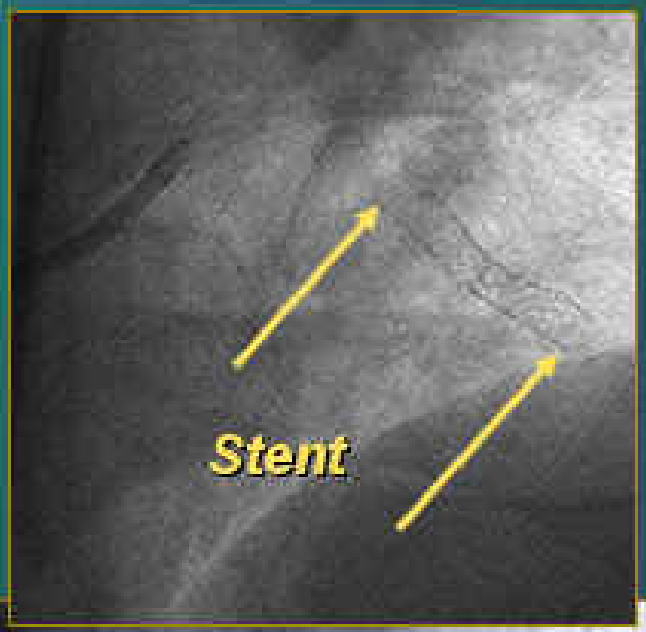


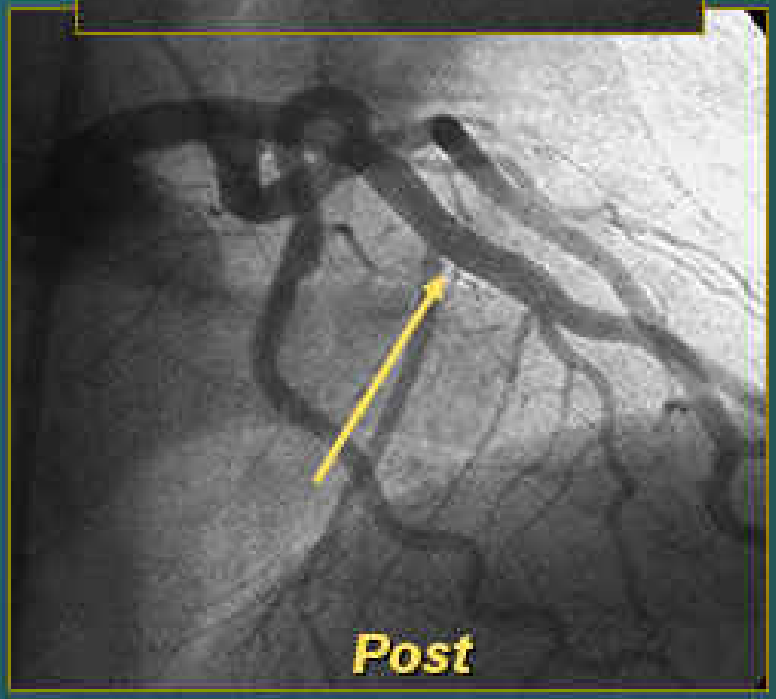




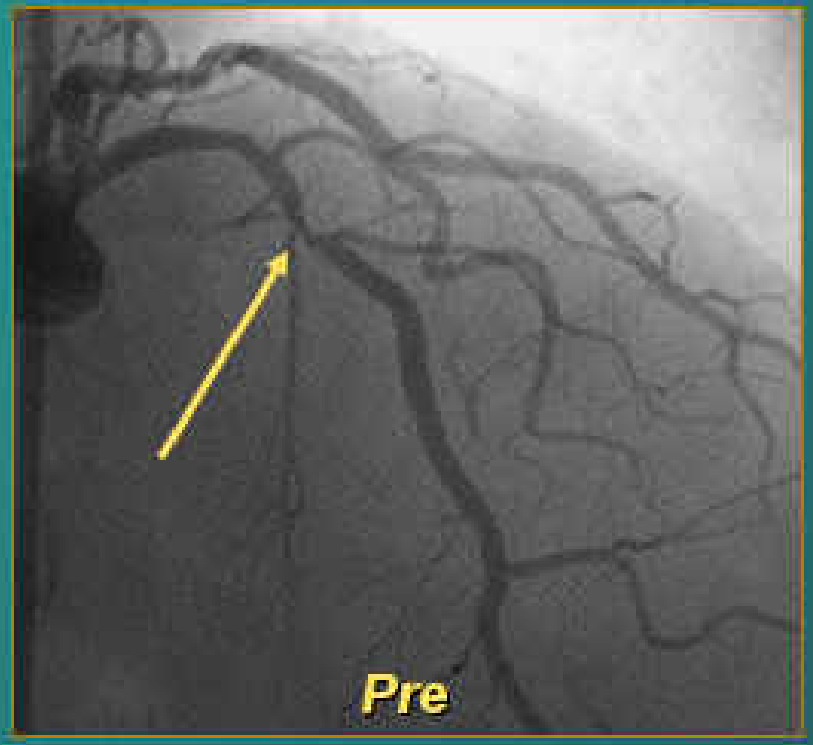
Case #3

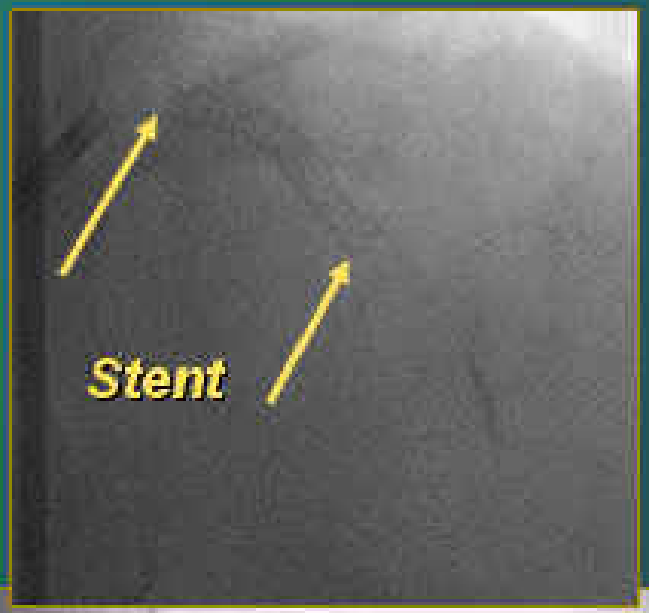


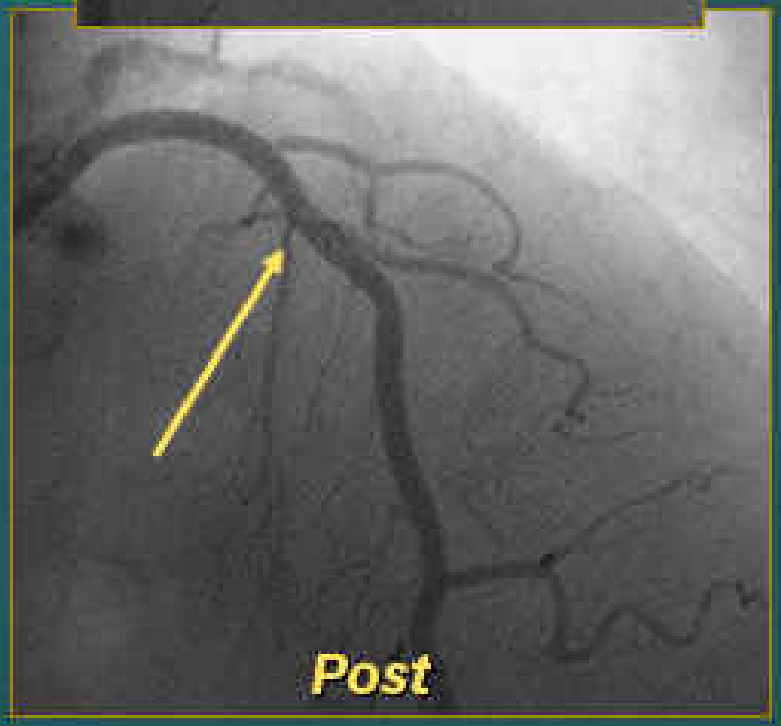




Case #5

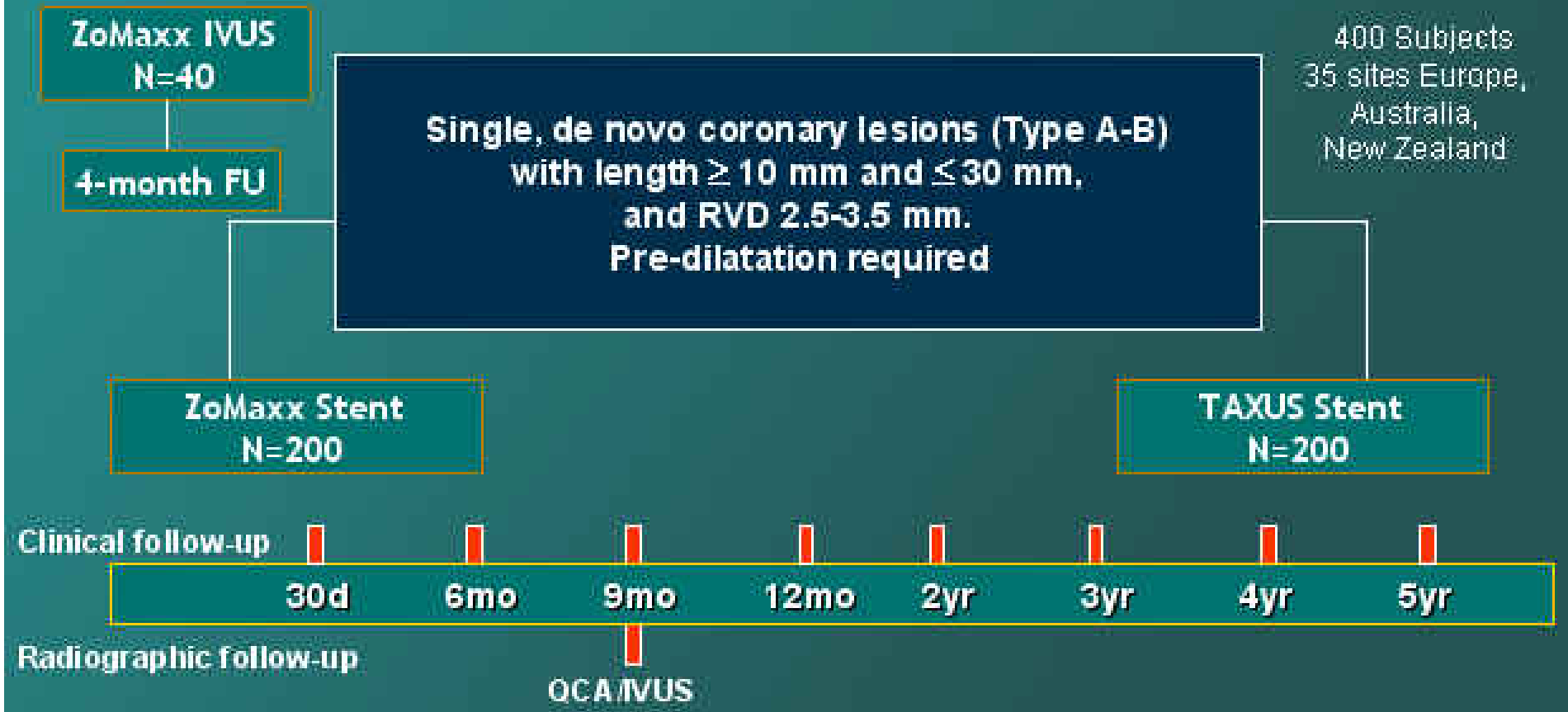






Case #6

ZoMaxx I (OUS Trial) Randomized, Non-inferiority Trial, Angiographic Endpoint



Primary Endpoint:	9-mos. in-segment late loss with equivalency limit of 0.25 mm, $\sigma = 0.4$ mm; > 99% power; 1-sided $\alpha = 0.05$
Secondary Endpoints:	MACE, TVF, TLR, TVR, binary restenosis, in-stent late loss, neointimal volume

New DES Systems

- Estradiol-Eluting Stent
- Biolimus A9-Eluting Stent
- Paclitaxel-Eluting Conor Stent
- ZoMaxx ABT 578-Eluting Stent
- Pimecrolimus-Eluting Avantec Stent

Pimecrolimus Study Design

Pimecrolimus-Eluting Duraflex Stent

Final results: TCT 2005

First In-Man
Dose Response Safety Trial
4-arm randomized
n = 80

200 mcg (14 days)	300 mcg (30 days)	400 mcg (30 days)	Duraflex Control
n = 20	n = 20	n = 20	n = 20

Primary Endpoint:
Late Loss and IH at 4 Months