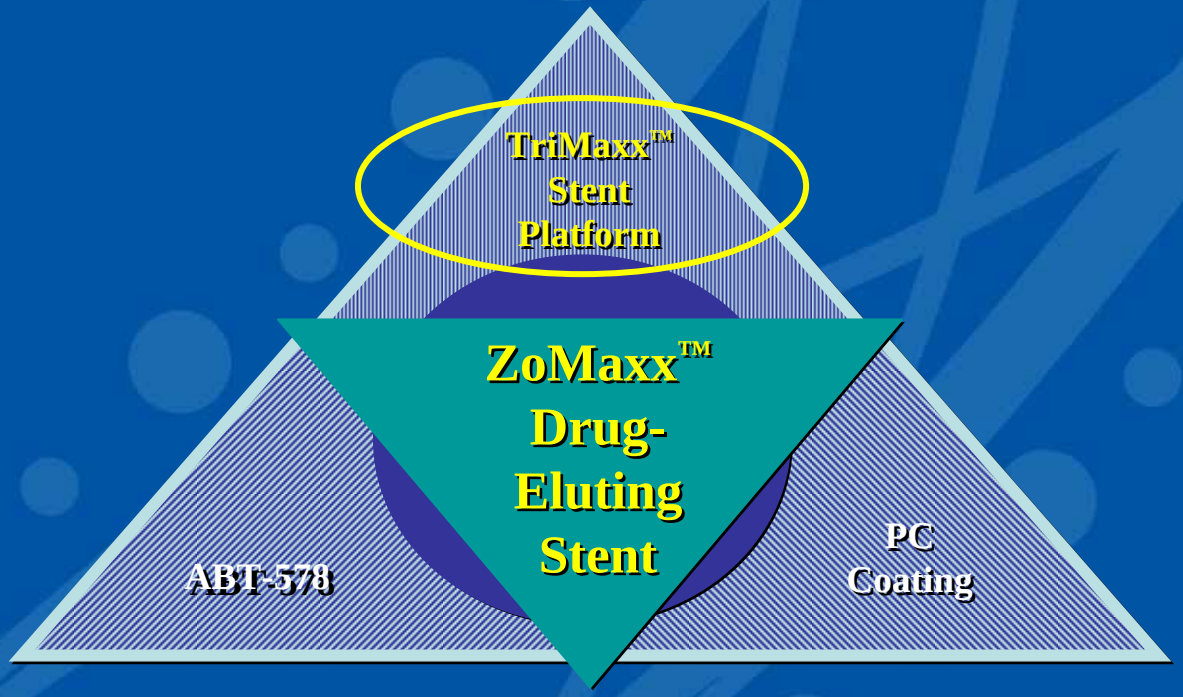
ABT 578 Elution from Phosphorylcholine: Zomaxx (Abbott)

Alan Yeung, MD
Professor of Medicine, Interventional Cardiology Chair,
Chief, Division of Cardiovascular Medicine (Clinical)
Stanford University School of Medicine

Stanford

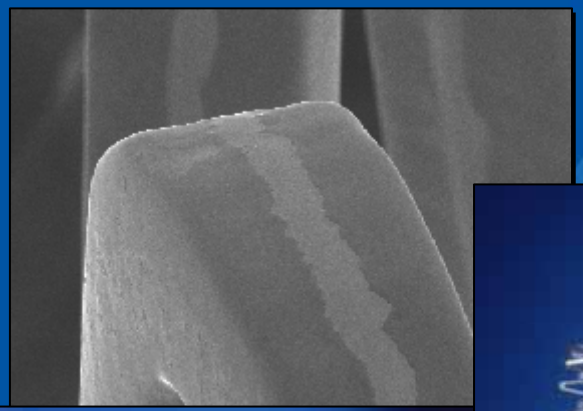
ZoMaxx: Stent Platform



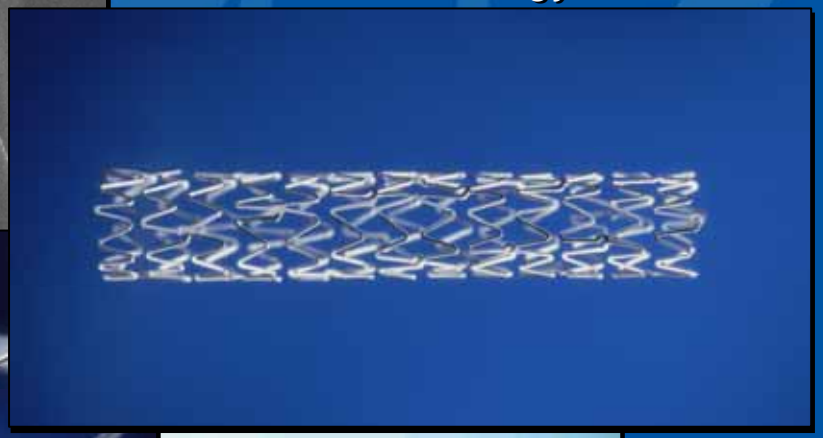
ZoMaxx™

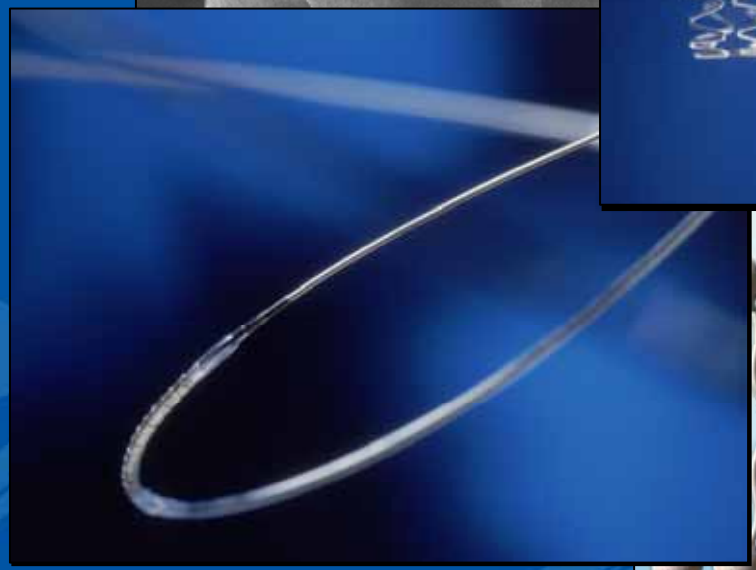
TriMaxx Coronary Stent

Triplex™ Material

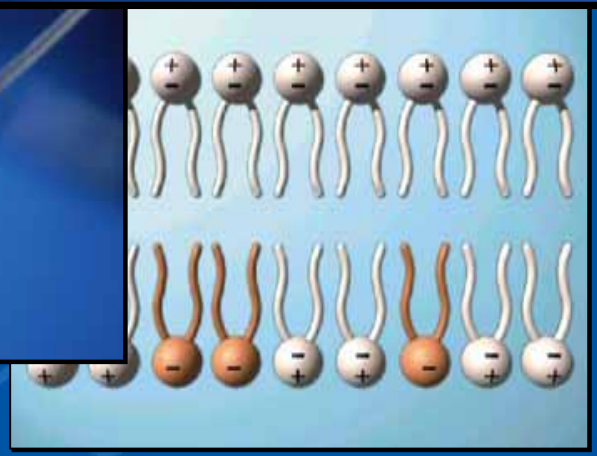


O.C.C.™ Technology





Stent Delivery Catheter



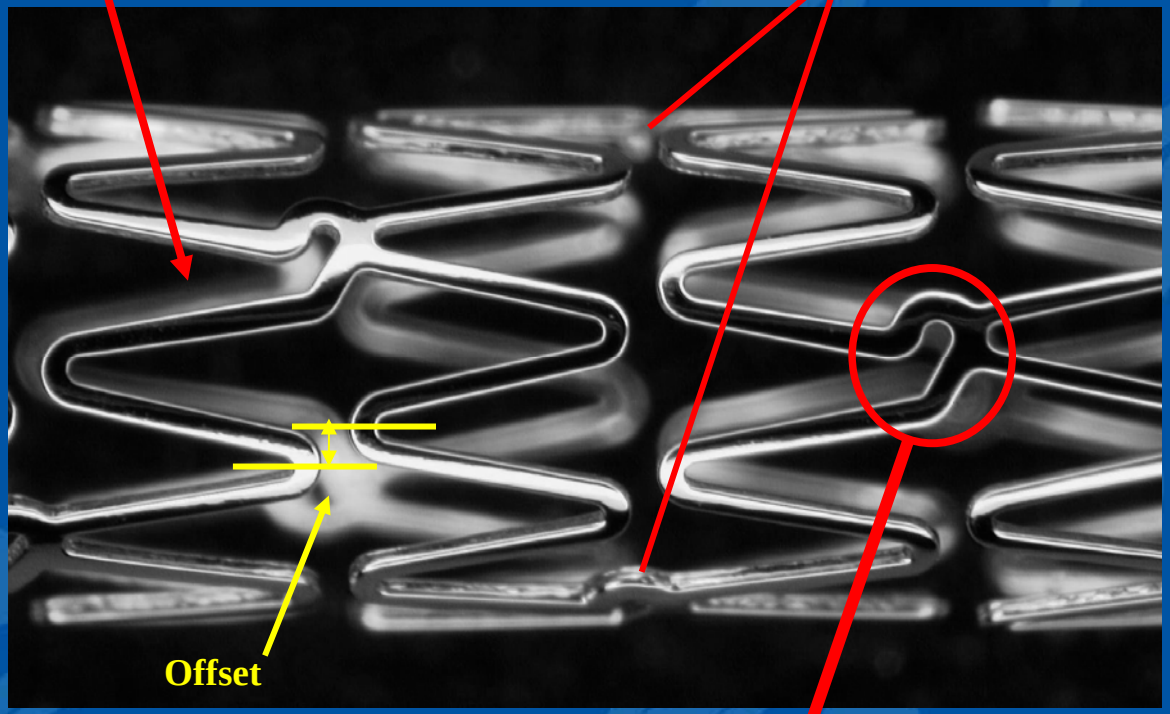
PC Technology™

ZoMaxx™

TriMaxx Stent Pattern

8 or 10 cells around perimeter
for optimum scaffolding

2 connectors between rings
for optimum flexibility

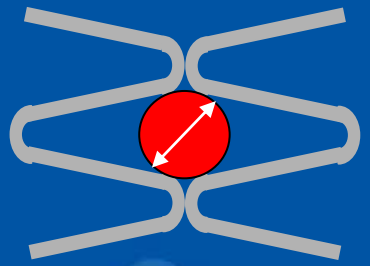


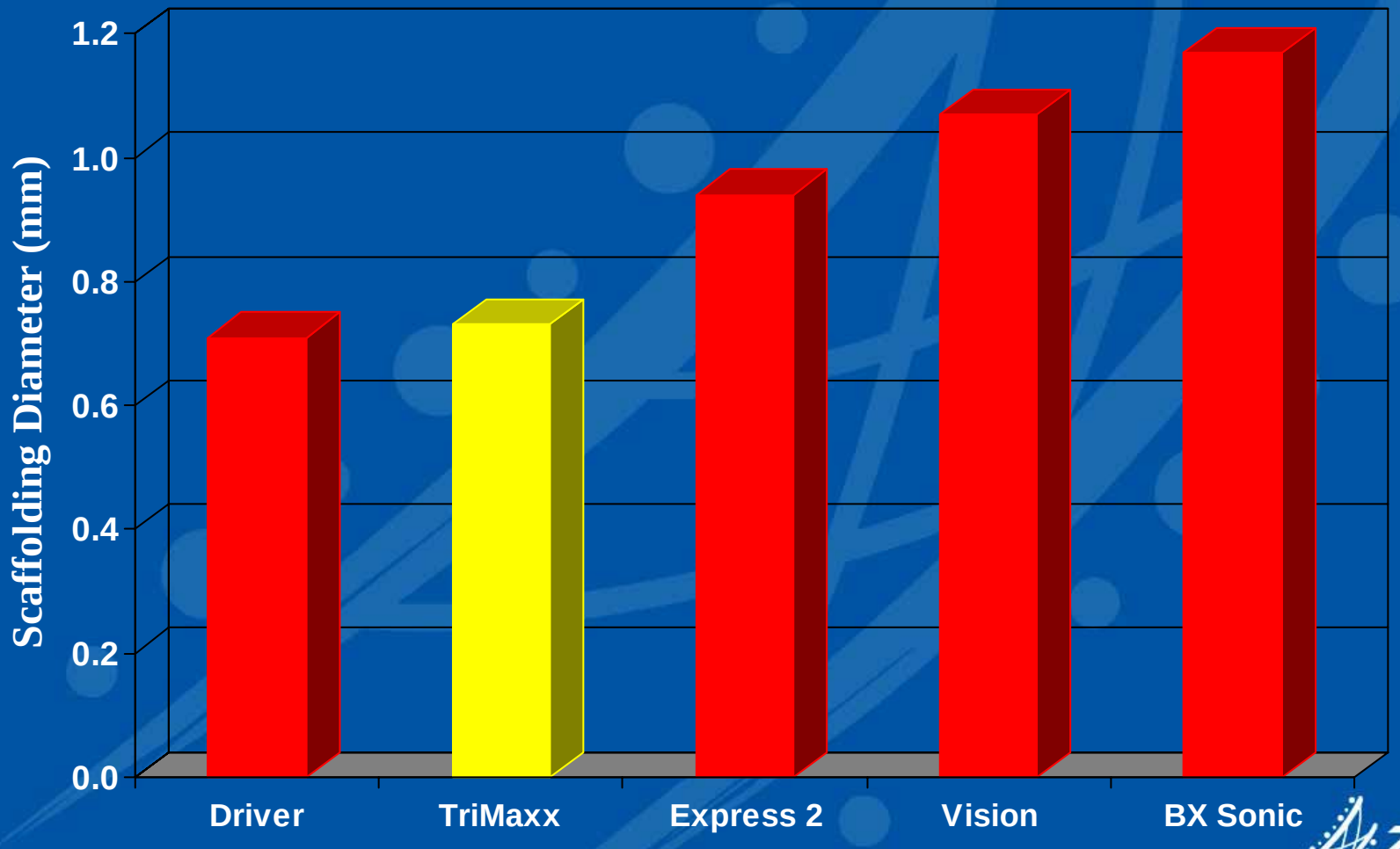
O.C.C.™ (Offset Crown Connector): proprietary connecting foot pulls the rings closer together and offsets the apexes of the crowns for improved scaffolding

Distal →

ZoMaxx

Stent Scaffolding
(Mean interstrut diameter)





ZoMaxx™

Driver is a trademark of Medtronic; Express² is a trademark of Boston Scientific;
Vision is a trademark of Guidant; Bx Sonic is a trademark of Johnson & Johnson

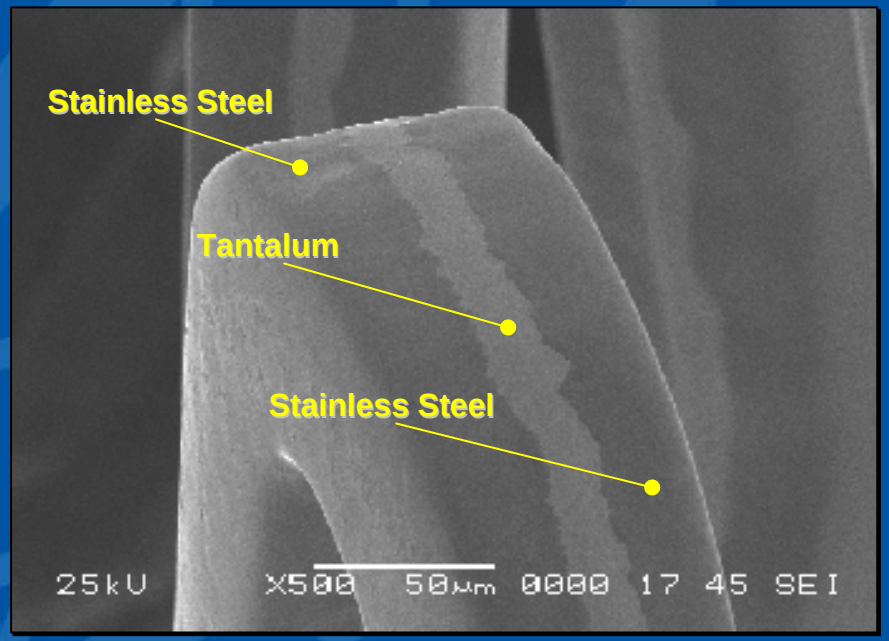
Data on file at Abbott Vascular Devices

Triplex Stent Material

Stainless Steel/Tantalum/Stainless Steel Composite

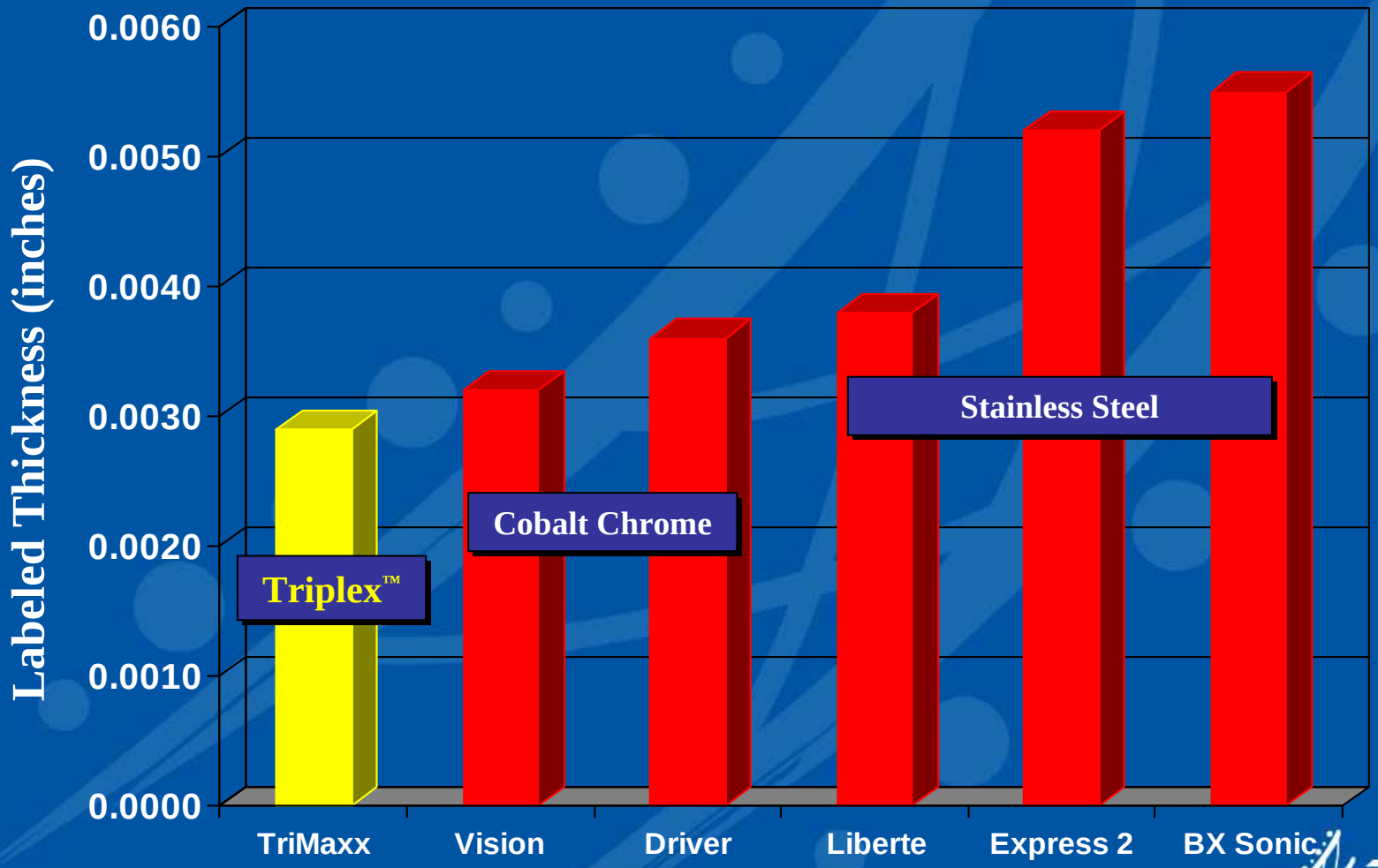
- 0.0007” Tantalum layer
- 0.0029” strut thickness

= **0.074mm**



ZoMaxx™

Stent Material and Strut Thickness



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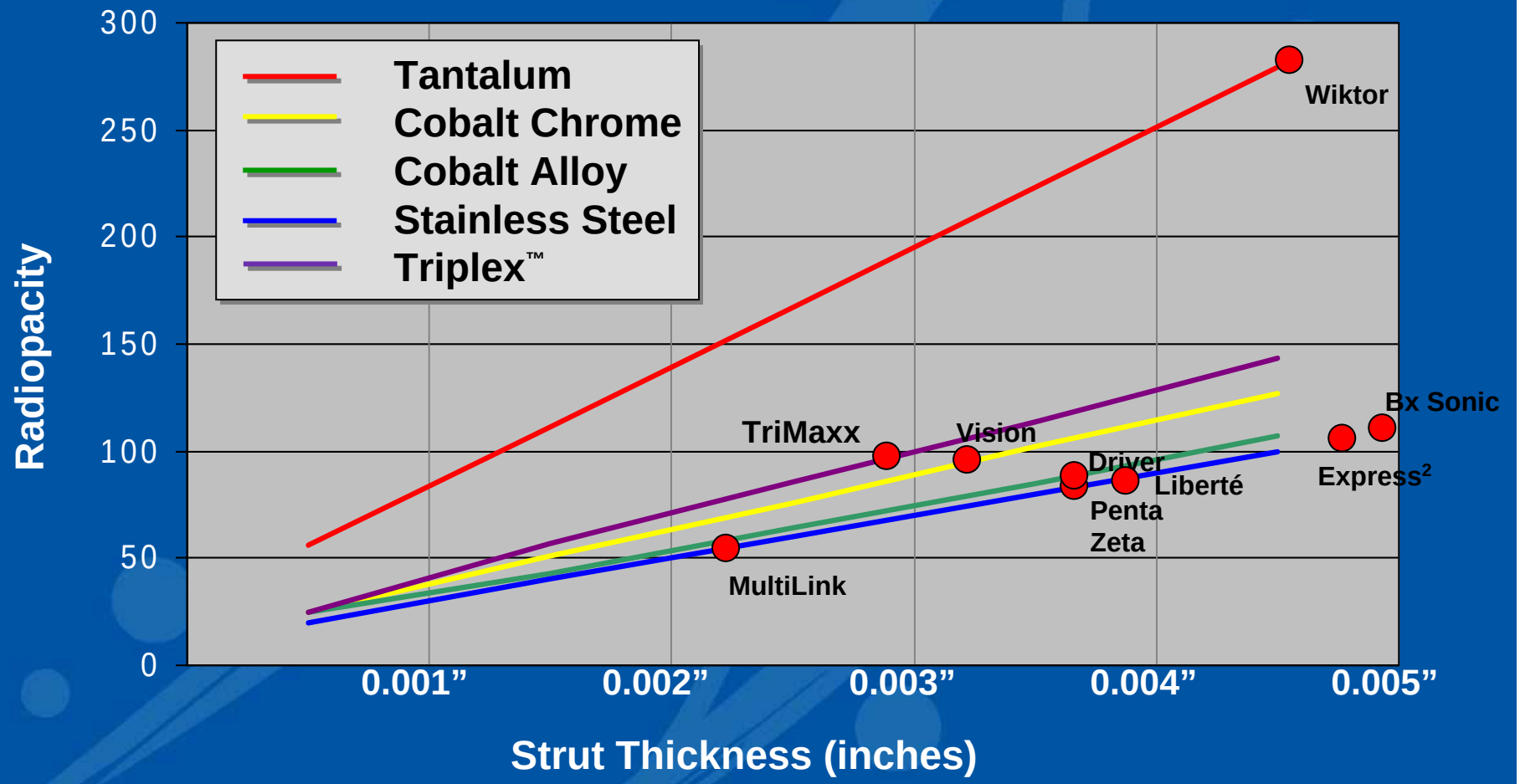
Data on file at Abbott Vascular Devices

Radiopacity



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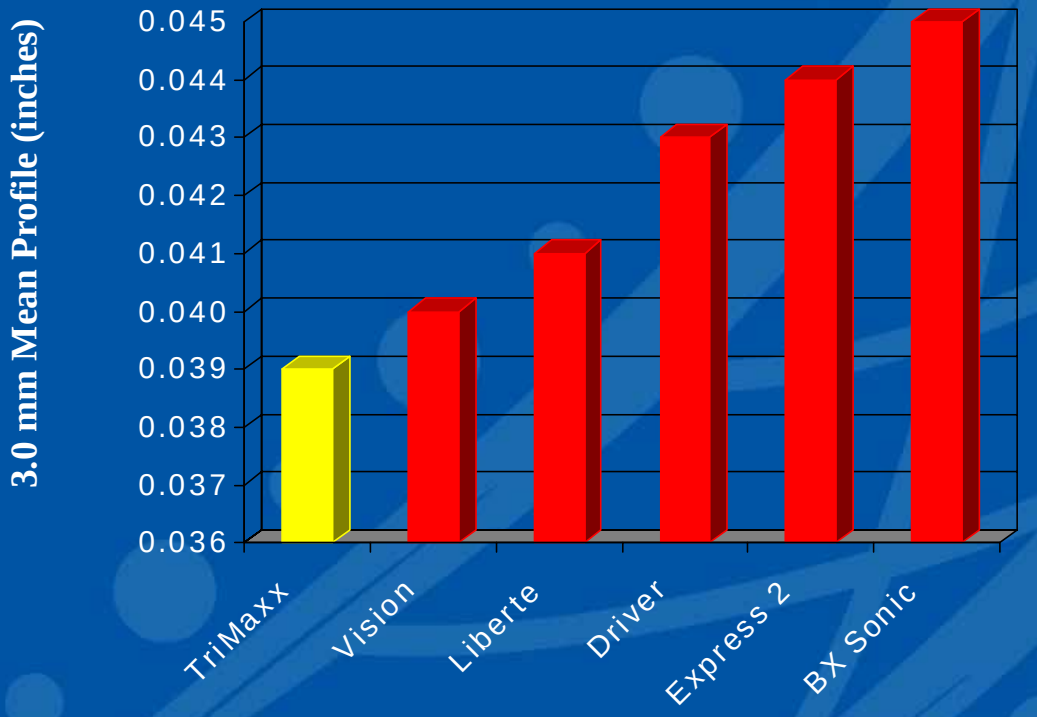
ZoMaxx™

Data on file at Abbott Vascular Devices

Crimped Stent Crossing Profile



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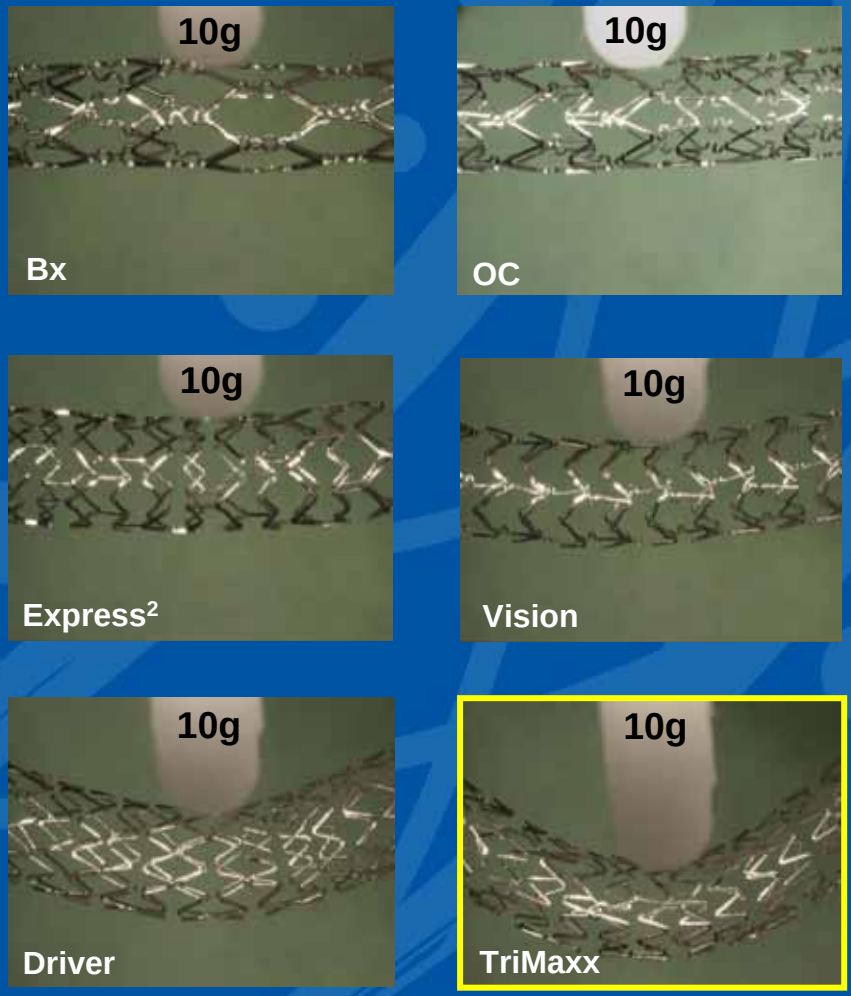
ZoMaxx™

Data on file at Abbott Vascular Devices

Stent Flexibility

In Vitro Bench Testing



ZoMaxx™

Driver is a trademark of Medtronic; Express² is a trademark of Boston Scientific;
Vision is a trademark of Guidant; Bx Sonic is a trademark of Johnson & Johnson

Data on file at Abbott Vascular Devices

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

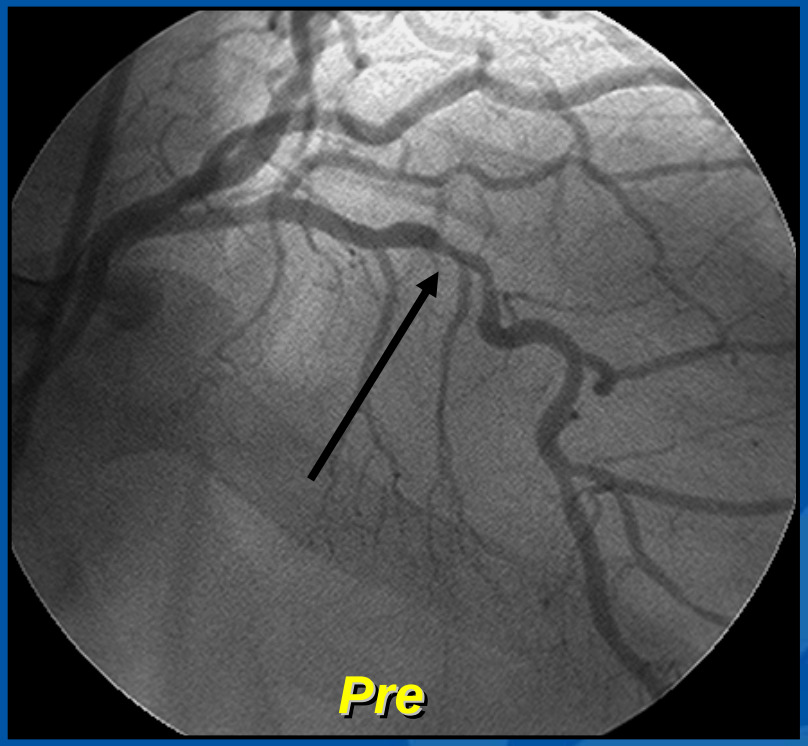
Stent Diameters	Stent Lengths
3.0 mm	18 mm
3.5 mm	18 mm

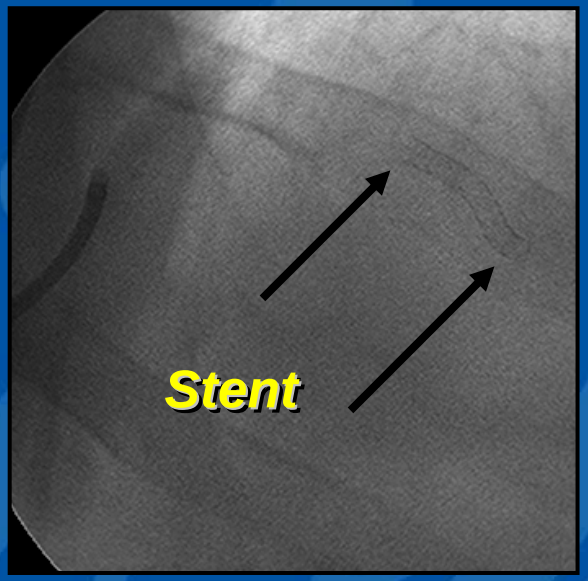
100 Subjects

Up to 5 Sites
– Brazil
– Germany

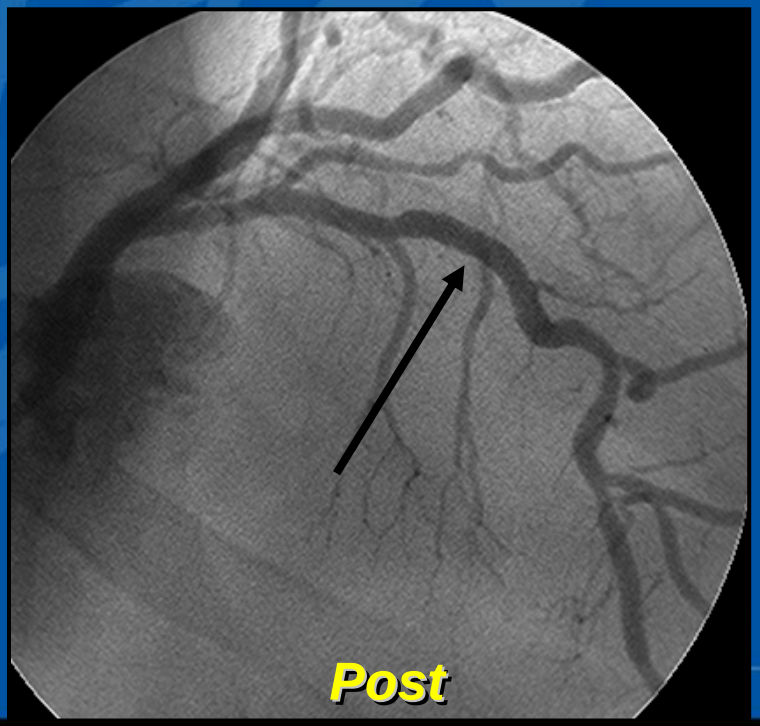
Primary Endpoint:	MACE at 30 days
Secondary Endpoints:	MACE, TLR, TVR, ABR, Late Loss at 6 months
Platelet Inhibition:	Clopidogrel/Ticlid (30 days), ASA 100 mg cont.

ZoMaxx

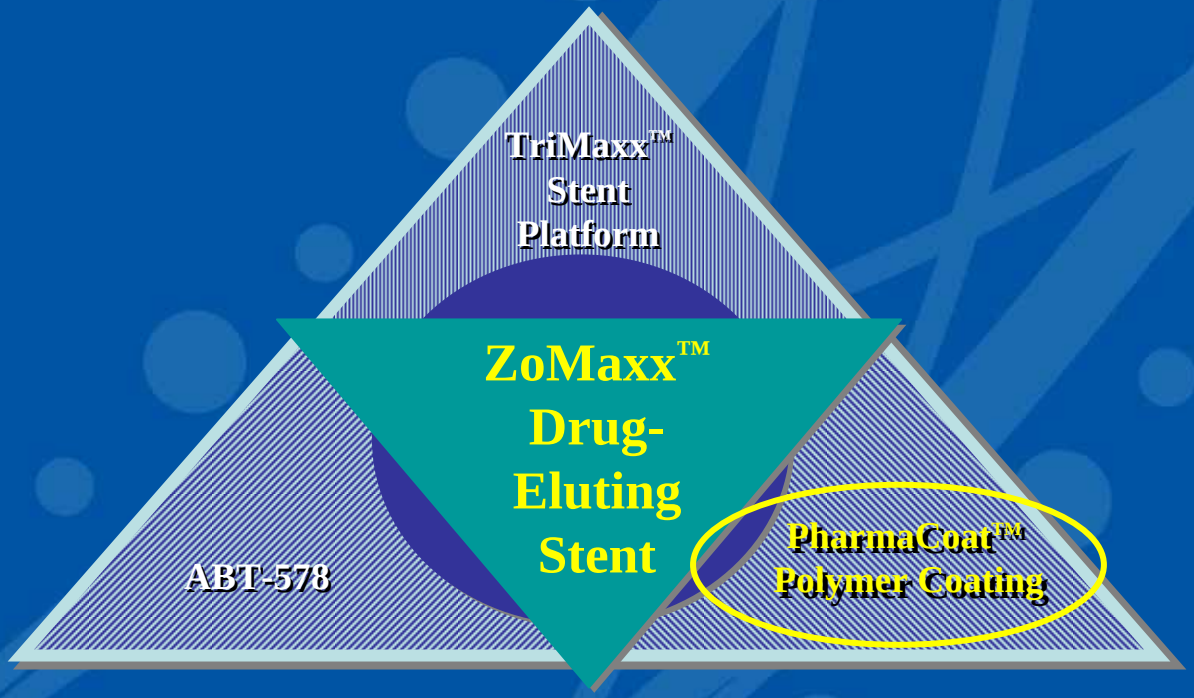




Case #1



ZoMaxx: Polymer

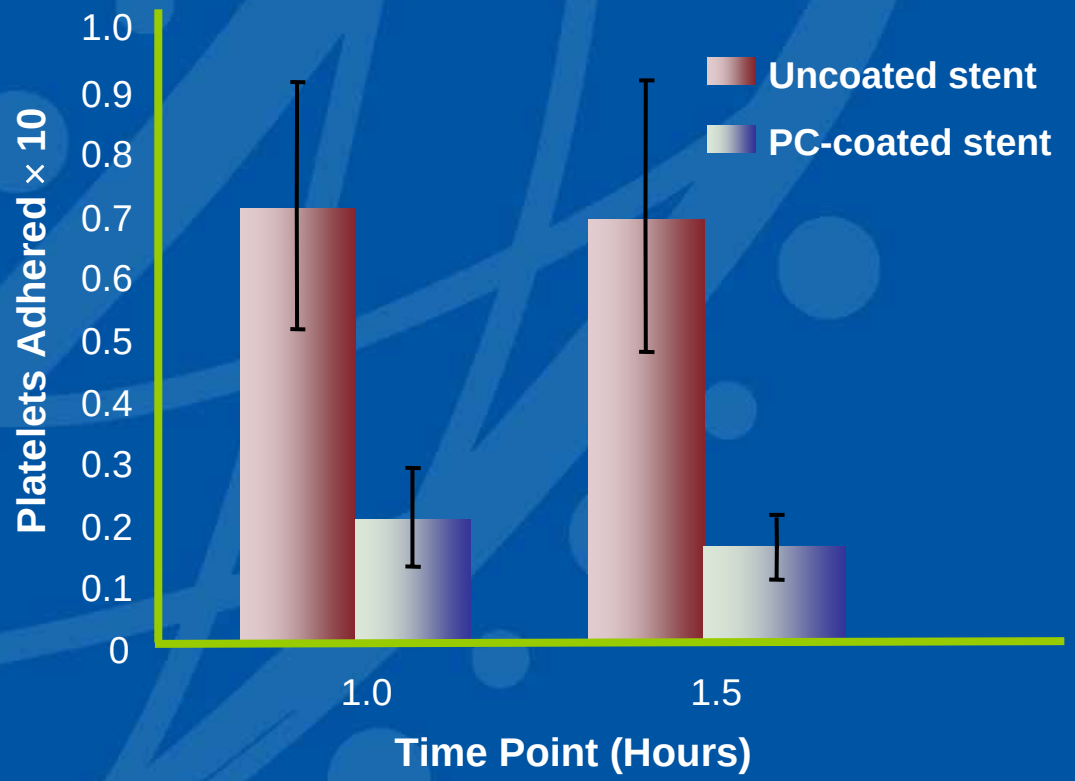


ZoMaxx

Polymer

PC Technology™ – Thrombo-Resistant

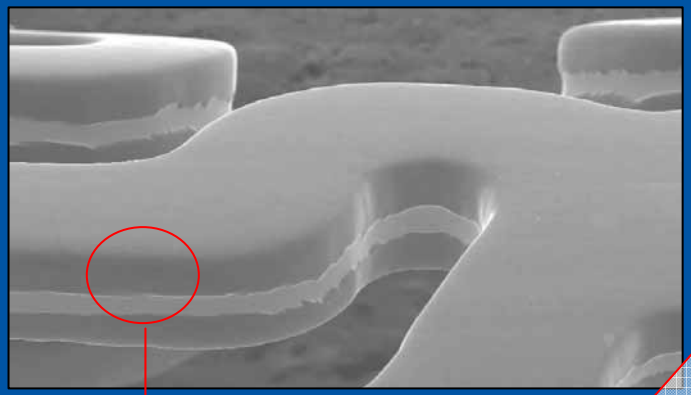
- Non-thrombogenic (hemocompatible)
  - Non-inflammatory
  - Hydrophilic: Inhibits protein adhesion
- PC coated stents showed significantly less platelet adhesion compared to uncoated stents

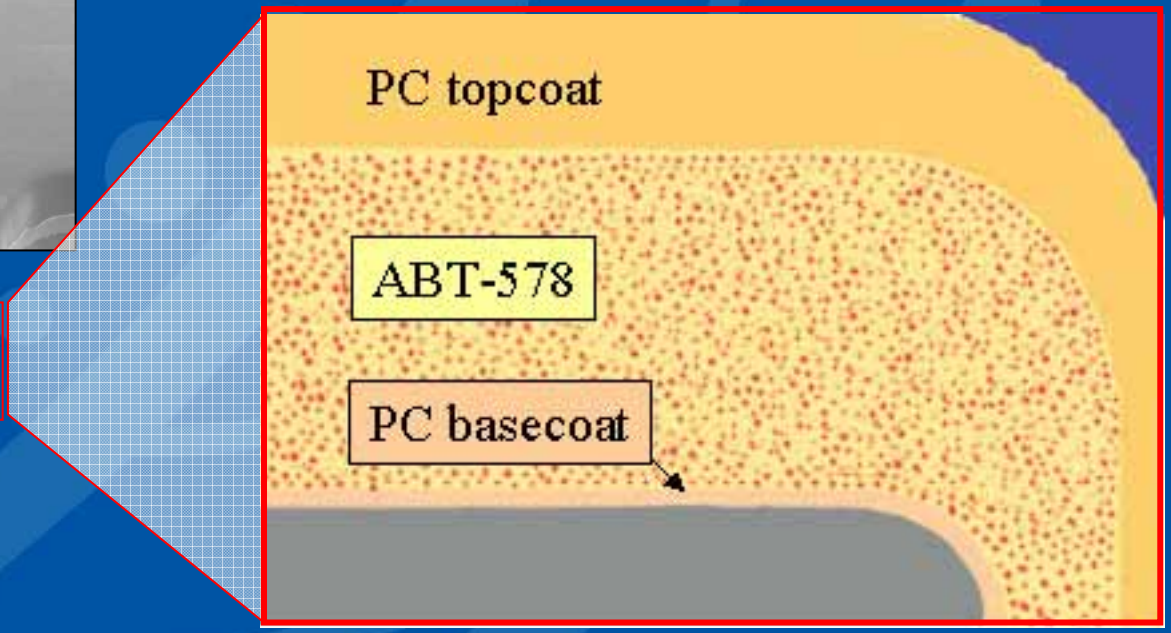


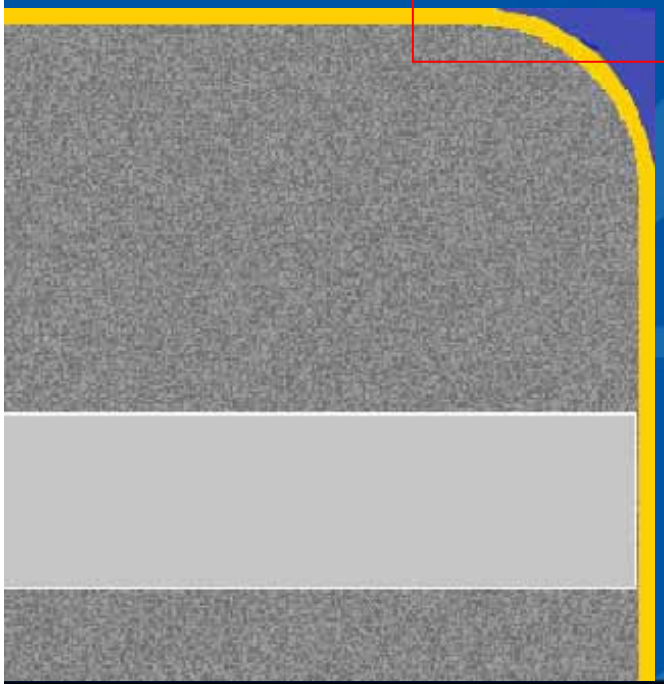
Lewis AL, *Coll Surf B; Biointerfaces*, 2000, 18, 261
(Baboon-Shunt Flow Model)

ZoMaxx™

The ZoMaxx Stent - PharmaCoat







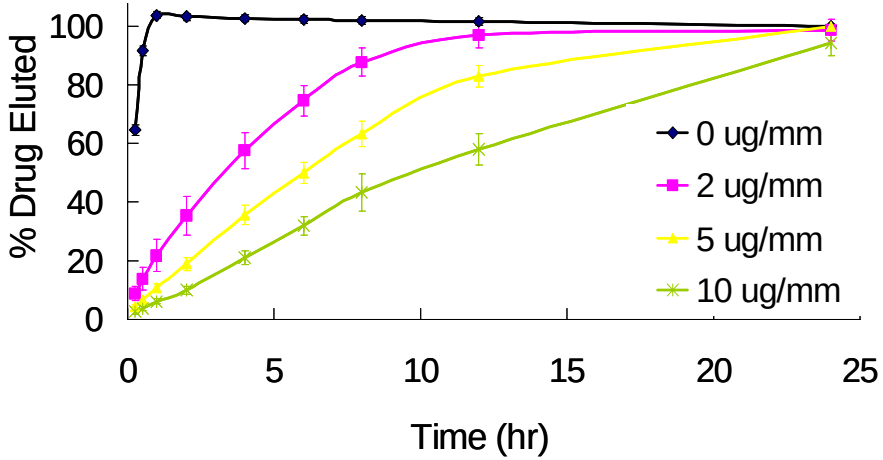
Not approved for sale in or outside the United States.

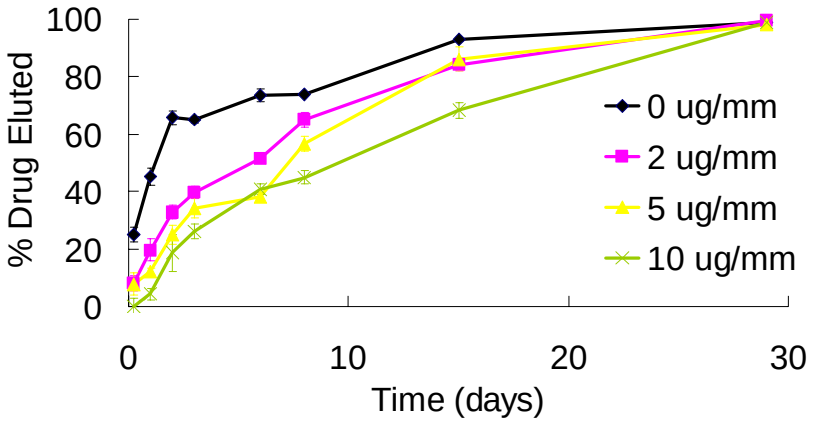
ZoMaxx™

The Effect of Adding a Polymer Topcoat on the Elution Rate from Drug-Eluting Stents

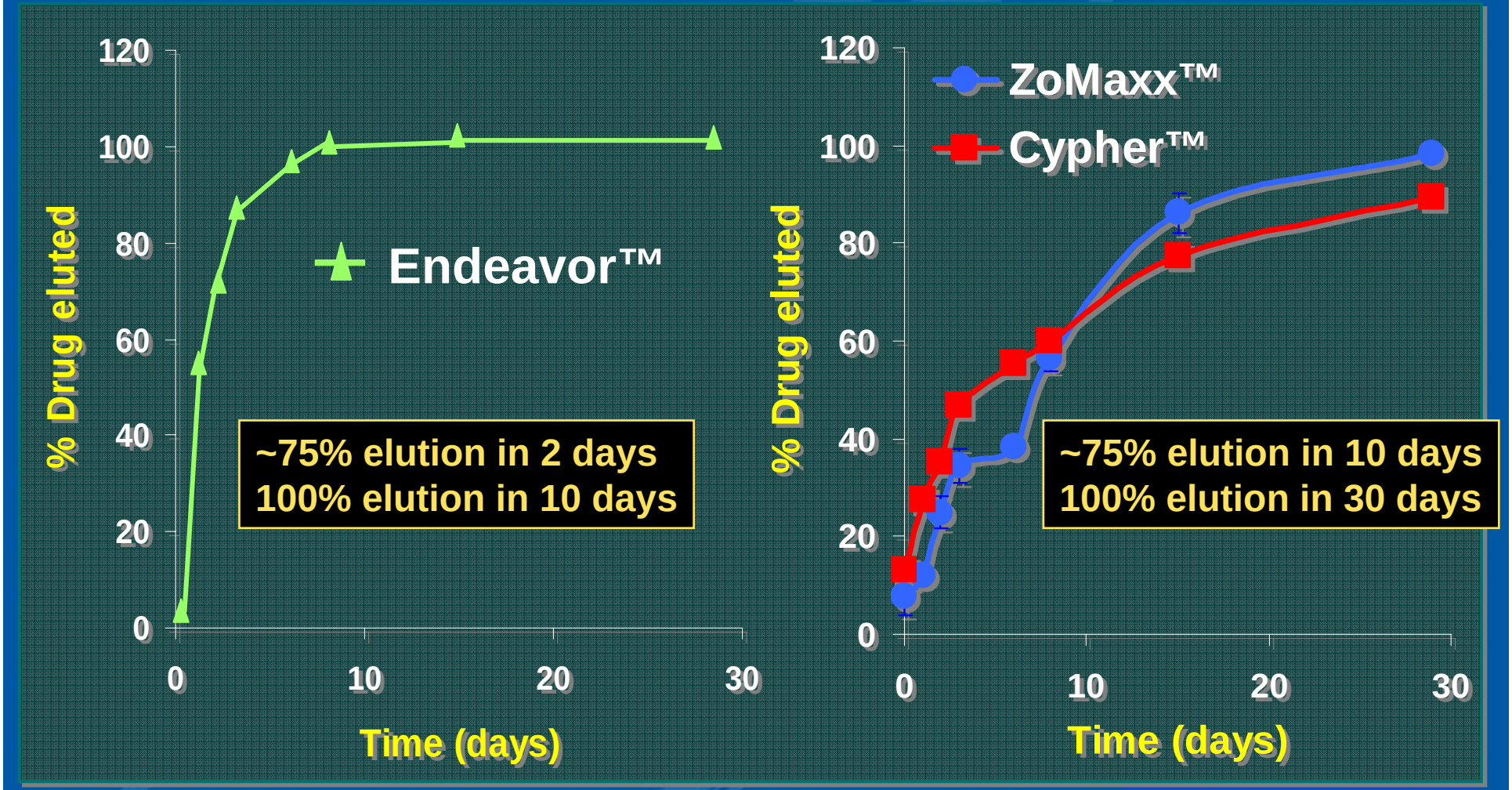
For *in vitro* testing, stents (n=12 per group) were placed in a 1% solution of solutol in acetate buffer, and aliquots removed at designated time points and assayed for ABT-578 via HPLC.

For *in vivo* testing, 128 stents (32 per group) were implanted in the common iliac arteries of New Zealand White rabbits and expanded to a 1:1.1 balloon-to-artery ratio. At set time (4 stents per group per time point), animals were euthanized, stents explanted, and the amount of ABT-578 remaining on the explanted stent was measured using HPLC.





Comparison of *in vivo* Elution Rates
Rabbit iliac models

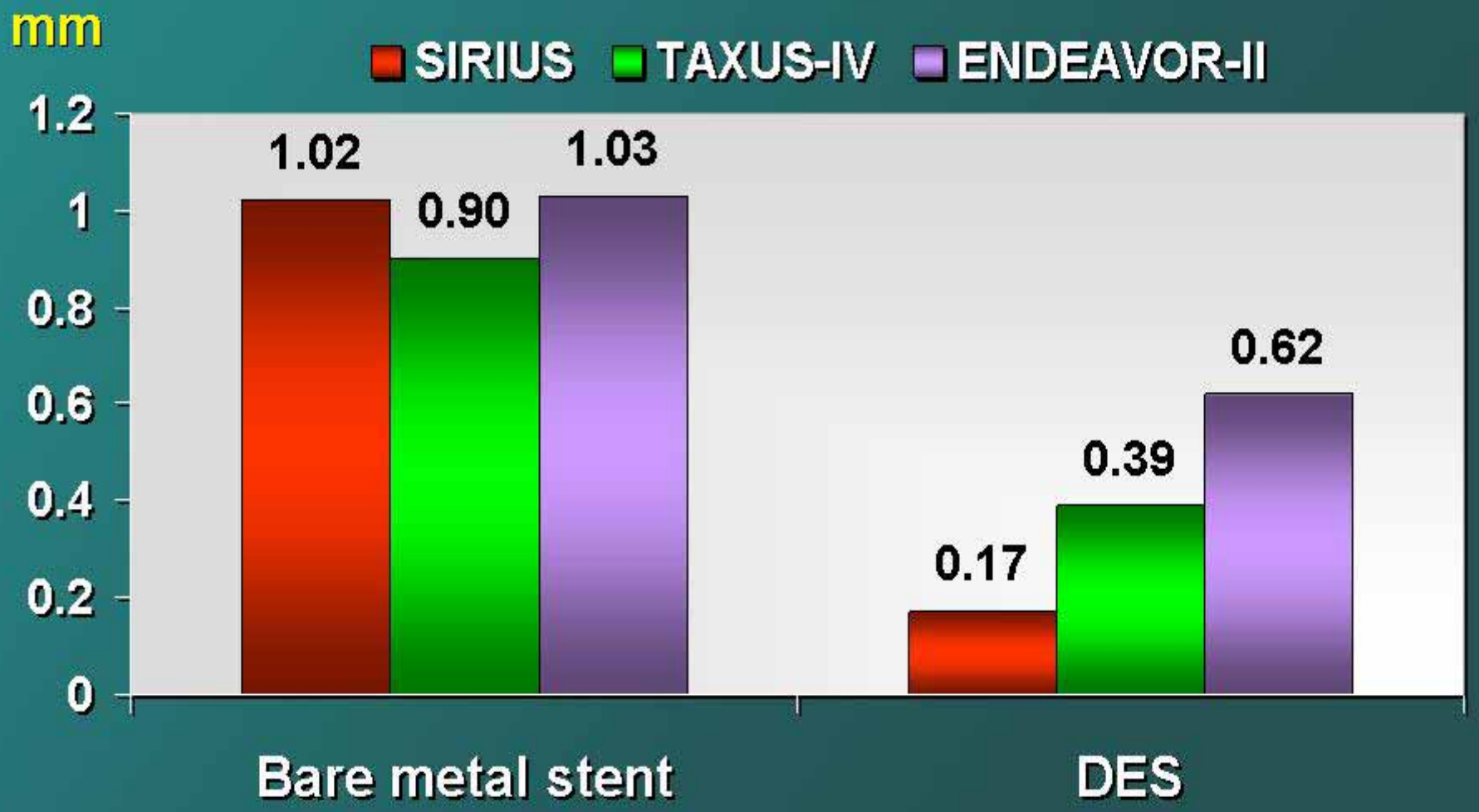


ZoMaxx and Cypher data from B. Chevalier, EuroPCR 2004
Endeavor data from G. Laarman, EuroPCR 2004

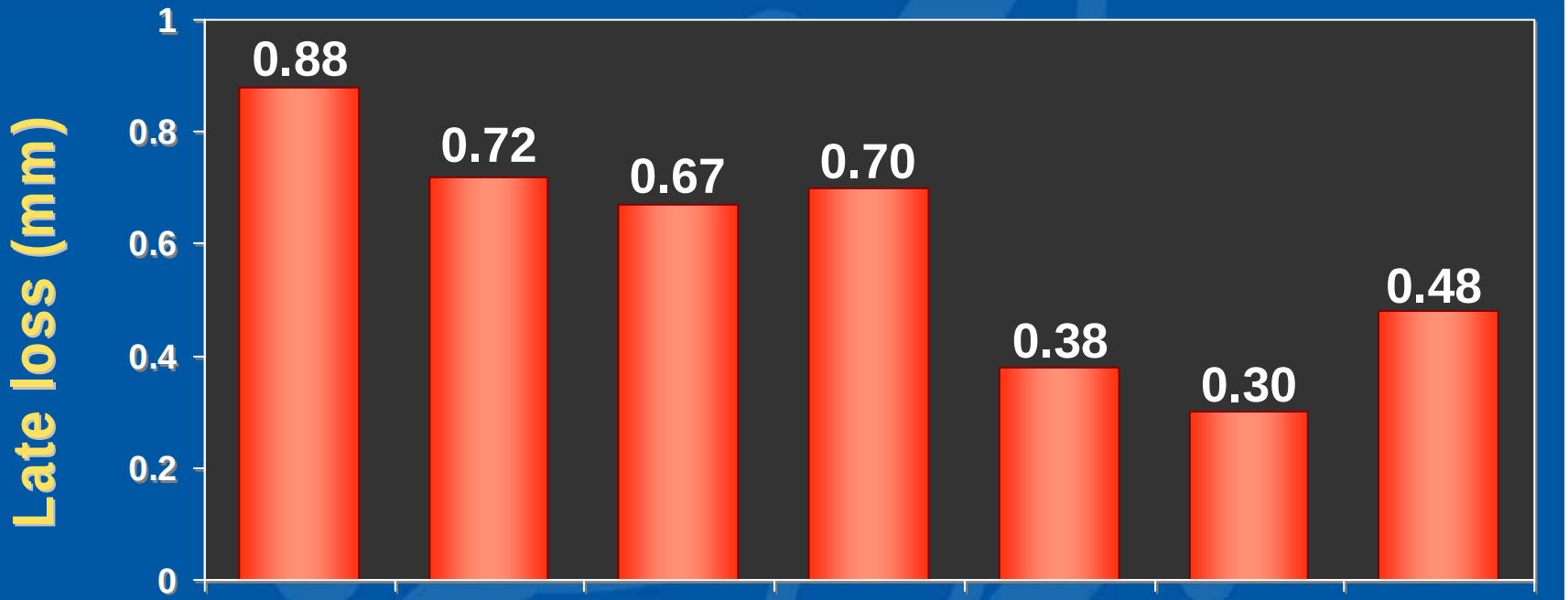
Stanford

ARE ALL DES THE SAME ?

Late loss (in-stent)



PISCES (n=221): QCA at 4 Months

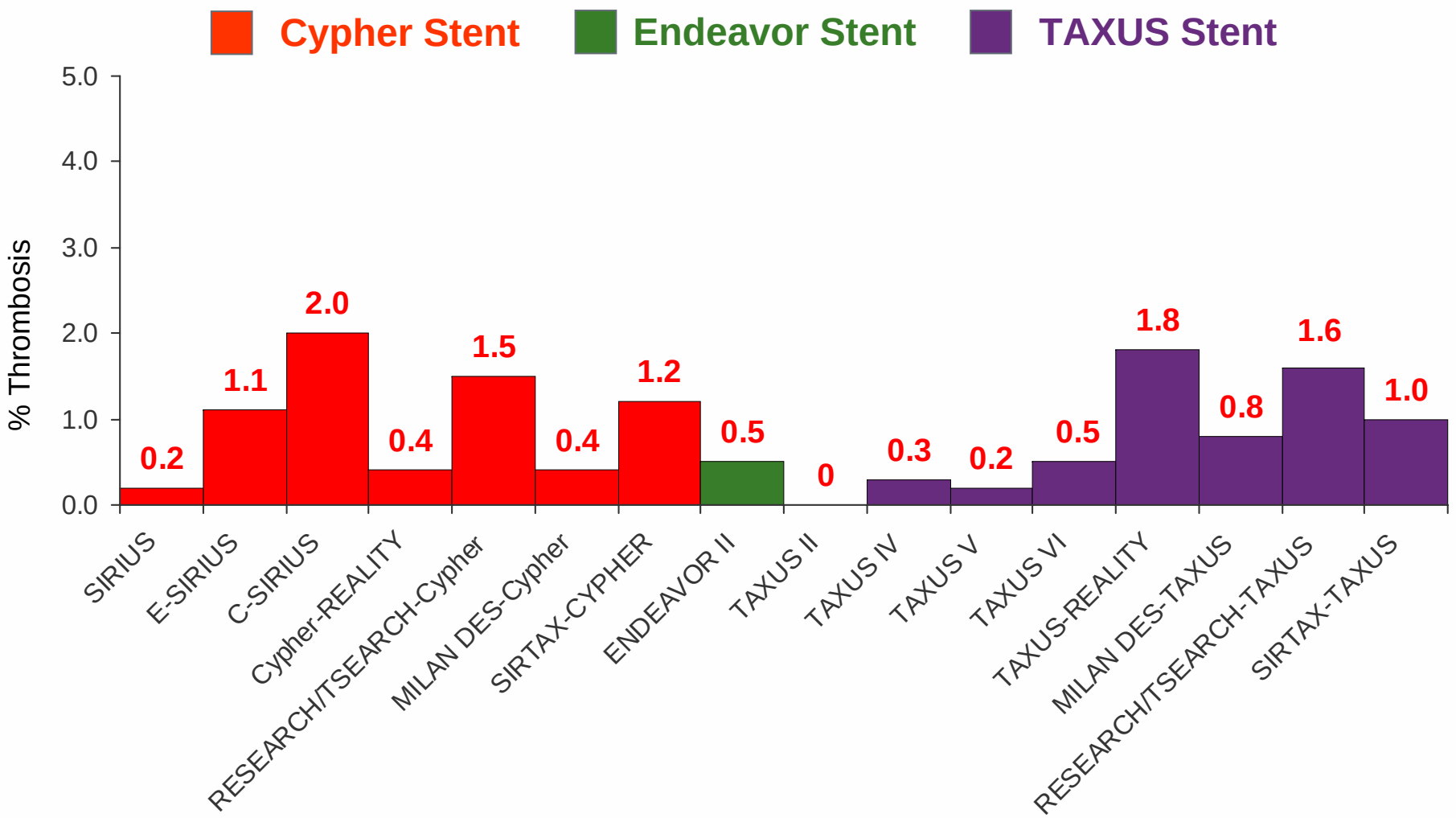


	D0	D1	D2	D3	D4	D5	D6
N	43	29	28	28	38	26	29
Dose (ug)	-	10	10	10	10	30	30
Release (d)	-	5	10	10	30	30	10

Stanford

SAT Rates Across Trials

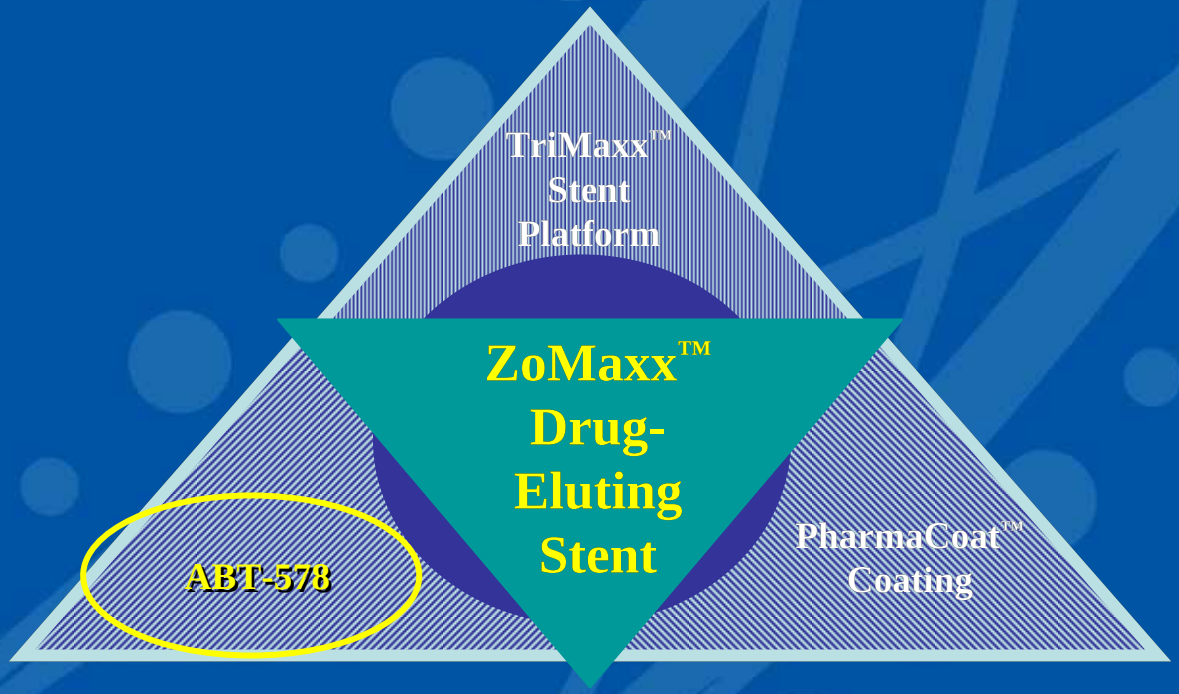
Out of Hospital to 30 Days



Data sources available on file.

TAXUS Stent = TAXUS® Express²™ Stent; Cypher is a trademark of Cordis Corp. ENDEAVOR is a trademark of Medtronic.

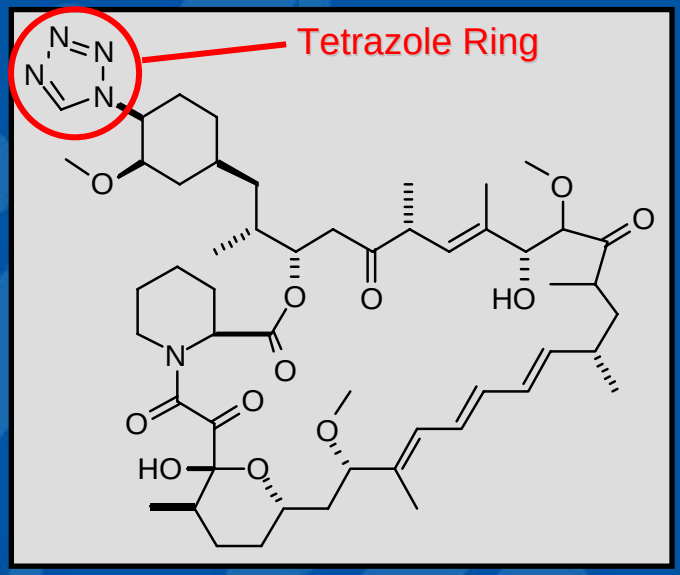
ZoMaxx: Drug Compound

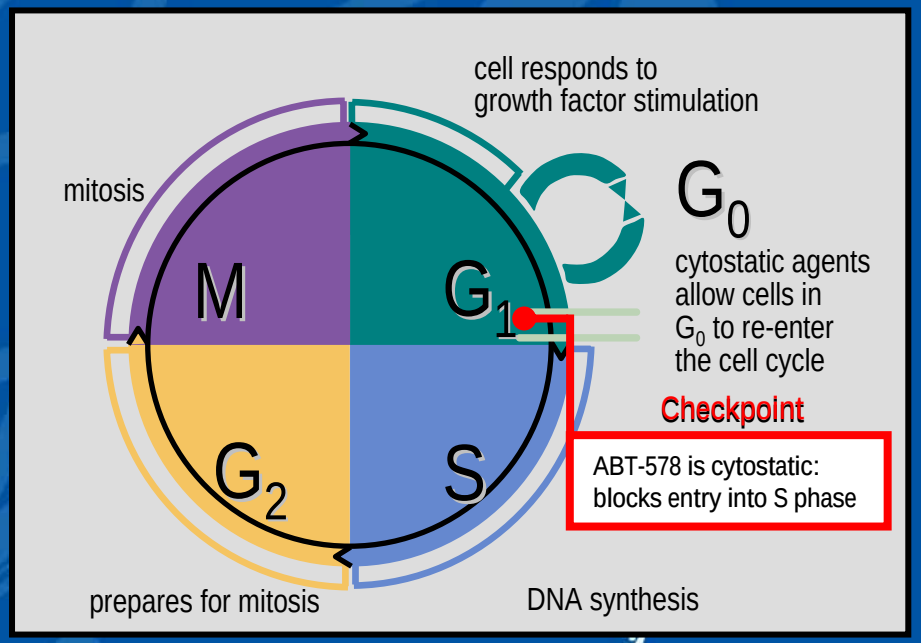


ZoMaxx™

ABT-578

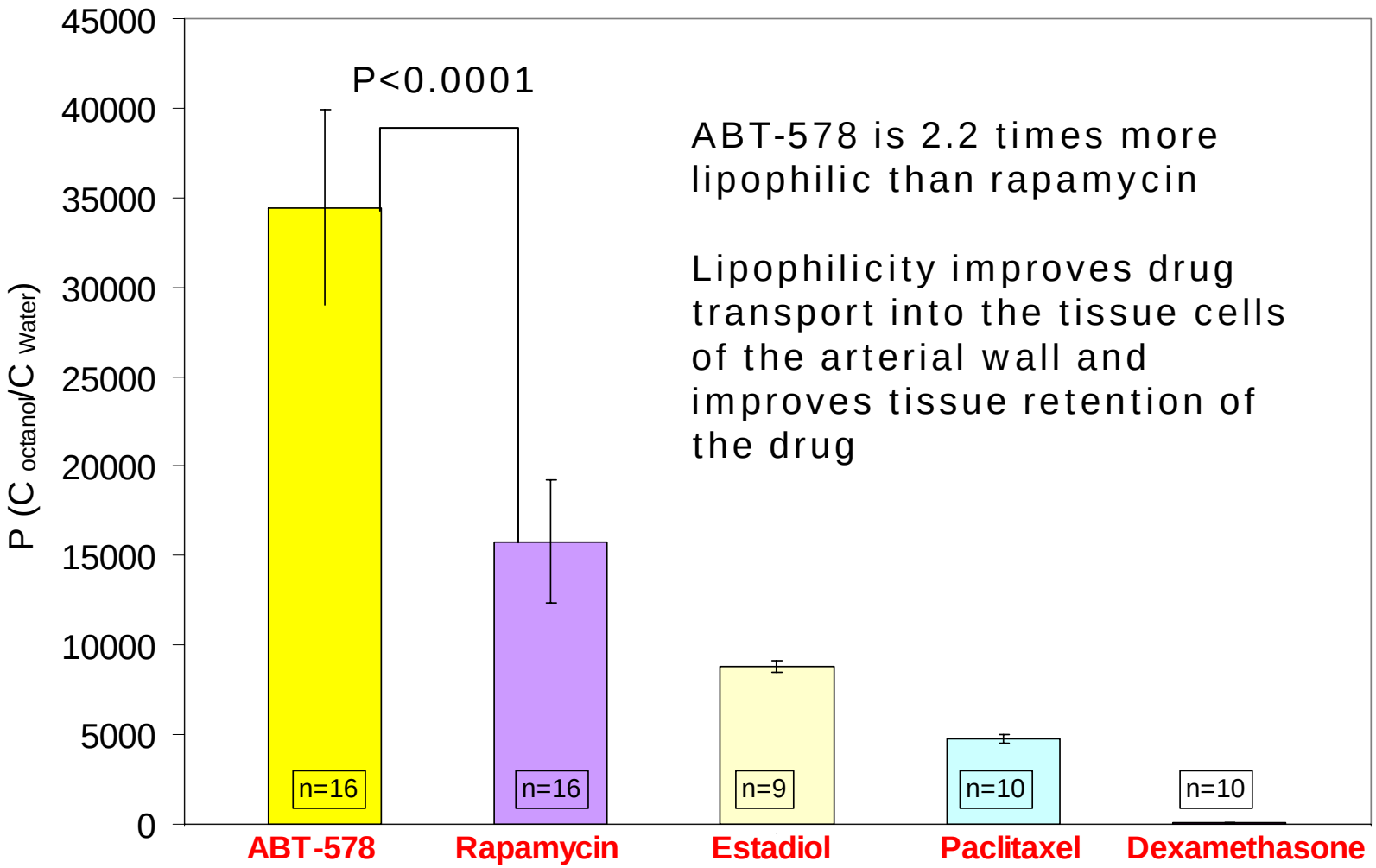
- ABT-578 is Abbott's proprietary compound for use on drug-eluting stents
- ABT-578 is structurally different from Sirolimus through the substitution of a tetrazole ring at the 42- position
- Delivered locally, ABT-578 inhibits inflammation and the proliferation of SMCs
- ABT-578 is cytostatic by halting the cell cycle in the late G_1 phase





ZoMaxx

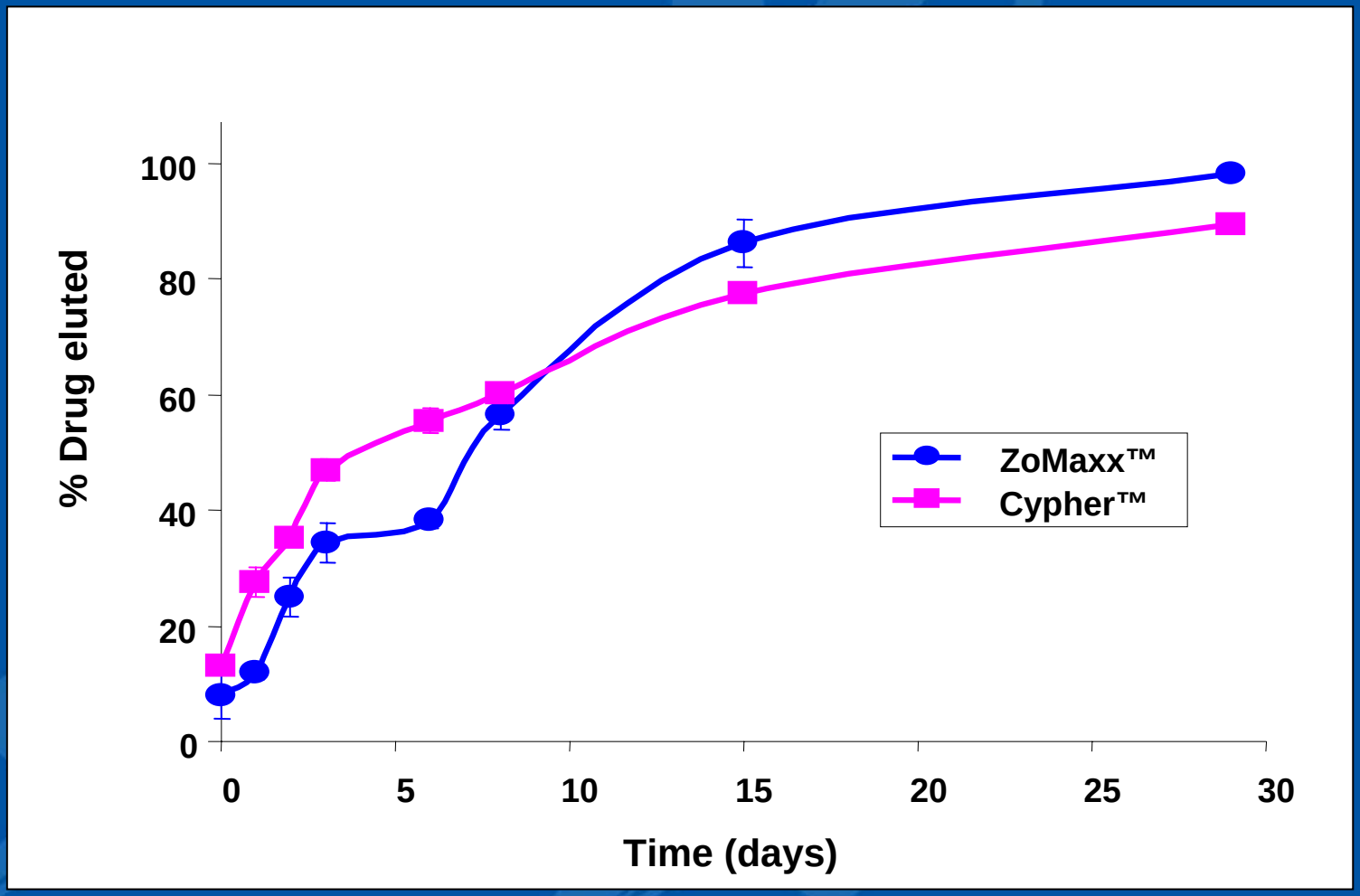
Lipophilicities of Some Clinical DES Agents



Determination of Partition Coefficients for ABT-578, Rapamycin, Paclitaxel, Dexamethasone, and Estradiol at 22 deg C, Abbott Laboratories Report on File, 2004

ZoMaxx

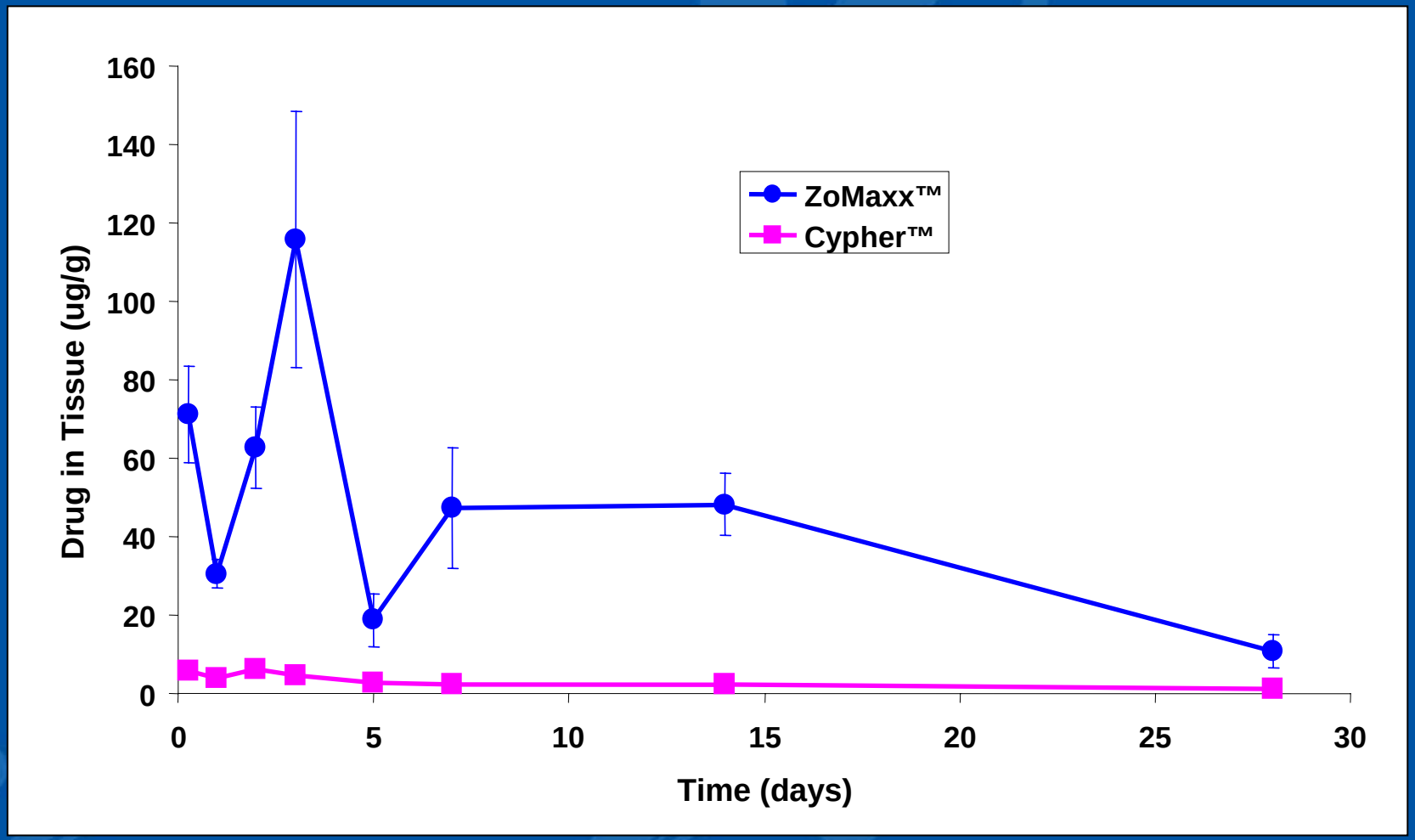
ZoMaxx™ Stent vs. Cypher™ Stent Drug Elution



A 28-day elution study to assess the tissue distribution of ABT-578 from polymer coated stents in rabbit iliac arteries; Study TE03-058; R&D/04/672; Data on file at Abbott Laboratories; n= 4 stents/timepoint; mean ± SEM; Cypher is a trademark of Johnson & Johnson; Results not indicative of clinical effectiveness.

ZoMaxx

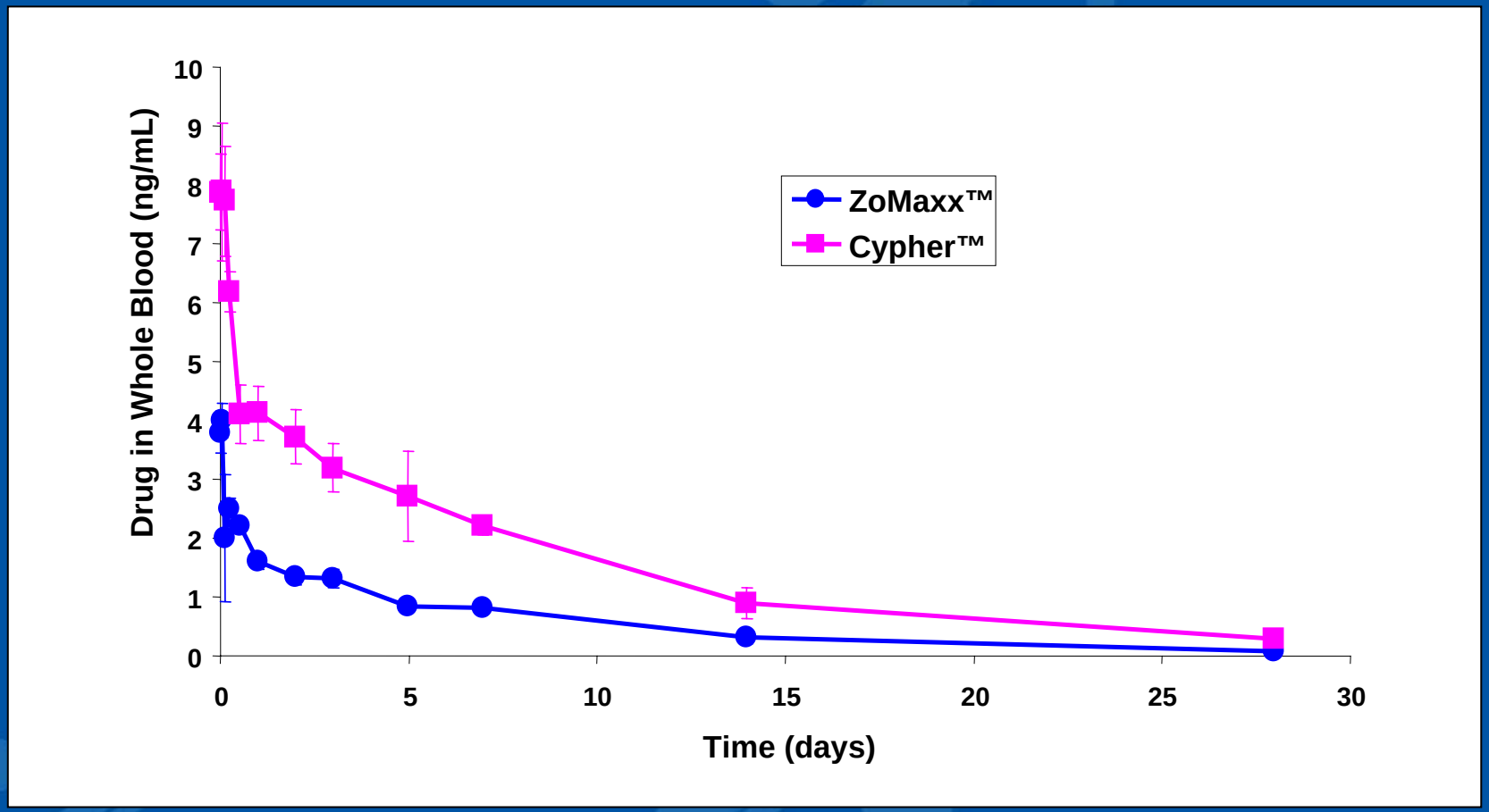
ZoMaxx™ Stent vs. Cypher™ Stent
Drug Penetration



A 28-day elution study to assess the tissue distribution of ABT-578 from polymer coated stents in rabbit iliac arteries; Study TE03-058; R&D/04/672; Data on file at Abbott Laboratories; n= 4 stents/timepoint; mean ± SEM; Cypher is a trademark of Johnson & Johnson; Results not indicative of clinical effectiveness.

ZoMaxx

ZoMaxx™ Stent vs. Cypher™ Stent
Whole Blood Drug Concentration



A 28-day elution study to assess the tissue distribution of ABT-578 from polymer coated stents in rabbit iliac arteries; Study TE03-058; R&D/04/672; Data on file at Abbott Laboratories; n= 4 stents/timepoint; mean ± SEM; Cypher is a trademark of Johnson & Johnson; Results not indicative of clinical effectiveness.

ZoMaxx

ABT-578 *in vivo* Porcine Evaluation – Mayo Clinic

- ABT-578 delivered from Bio*divYsio*® PC-coated stent in porcine coronary arteries

Control Stent: PC Coating only

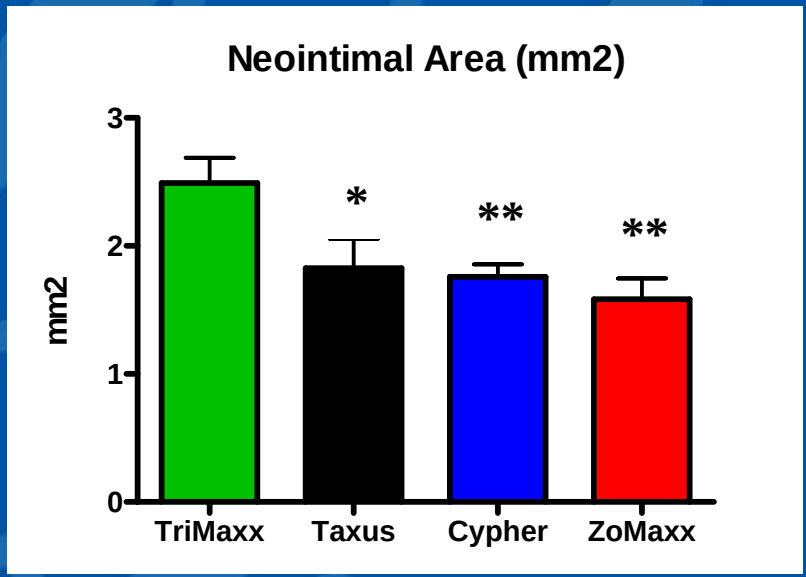
ABT-578 stent

Courtesy of Robert S. Schwartz, MD
Minneapolis Heart Institute Foundation

ZoMaxx™

Effect of TriMaxx, ZoMaxx, Cypher, and Taxus Stents on Swine Coronary Morphometry at 28 days (mean ± SEM)

- **18 animals received a single ZoMaxx, Cypher, and Taxus stent implanted in one of three randomized coronary arteries**
- **An additional 3 animals received 3 TriMaxx stents each**
- **Balloons were expanded to achieve a 1.3:1 stent:artery ratio**
- **After 28 days, the hearts were excised, the arteries perfusion-fixed at 100 mmHg, sectioned, and stained with hematoxylin and eosin for morphometric evaluation**



*p<0.05 vs. TriMaxx

**p<0.01 vs. TriMaxx

ABT-578, paclitaxel, and rapamycin-eluting stents show similar efficacy in a porcine model of coronary restenosis (abstract). Cardiovascular Revascularization Therapeutics 2005 (accepted). Data on file at Abbott Laboratories; n= 4 stents/timepoint; mean ± SEM; Cypher is a trademark of Johnson & Johnson; Taxus is a trademark of Boston Scientific.

ZoMaxx

ZoMaxx Clinical Programs

- ZOMAXX I
  - PI: Bernard Chevalier, MD
  - First patient enrolled 14 Sept 04 at St. Vincent's Hospital in Melbourne, Australia (Robert Whitbourn, M.D.)

bc8

- ZOMAXX II
  - PI: Alan Yeung, MD

ZoMaxx™

bc8 That seems very short about ZOMAXX II
Does Martin present somethingelse?
Bernard, 2004-05-12

ZOMAXX I Trial
Randomized, Non-inferiority Trial

Single, *de novo* coronary lesions (Type A-B)
with length ≥ 10 mm and ≤ 30 mm,
and RVD 2.5-3.5 mm.
Pre-dilatation required

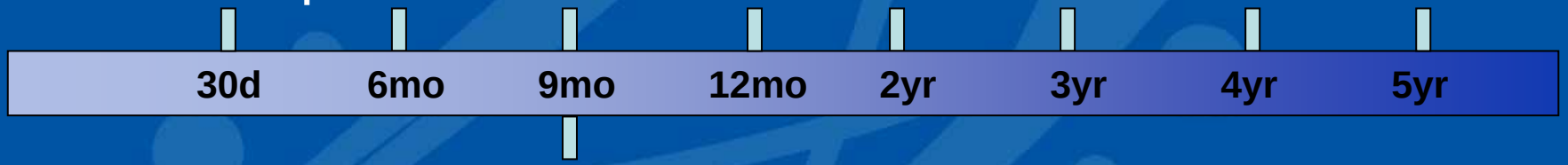
Stent Diameters	Stent Lengths
2.5 mm	8, 18, 23, 28 mm
3.0 mm	8, 18, 23, 33 mm
3.5 mm	8, 18, 23, 33 mm

N=400
34 sites
Europe
Australia
New Zealand

ZoMaxx™ Stent
N=200

TAXUS™ Stent
N=200

Clinical follow-up

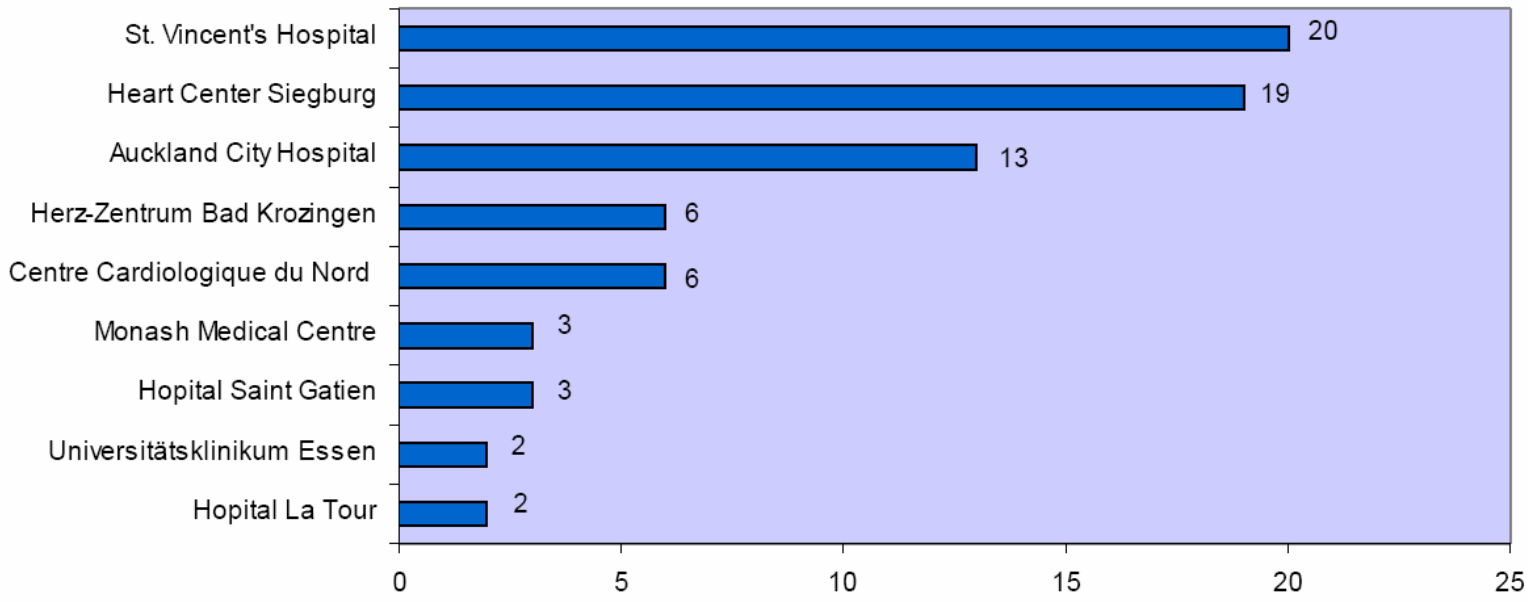


Radiographic follow-up **QCA/IVUS**

Primary endpoint:	**9-mos. in-segment late loss with equivalency limit of 0.25 mm, σ=0.4 mm; > 99% power; 1-sided α=0.05**
Secondary endpoints:	**MACE, TVF, TLR, TVR, binary restenosis, in-stent late loss, neointimal volume, neointimal volume obstruction**
Medications:	**Clopidogrel 75 mg QD for at least 6 months, ASA 100 mg QD ≥ 12 months**
Stratification:	**Site**

ZOMAXX I Trial
Randomized, Non-inferiority Trial

74 patients enrolled as of 11 February 2005



ZOMAXX

ZOMAXX II Trial

Randomized, Non-inferiority Trial, Clinical Endpoint

Single, *de novo* coronary lesions (Type A-B)
with length ≥ 10mm and ≤ 28mm
and RVD 2.5-3.75mm
Pre-dilatation required

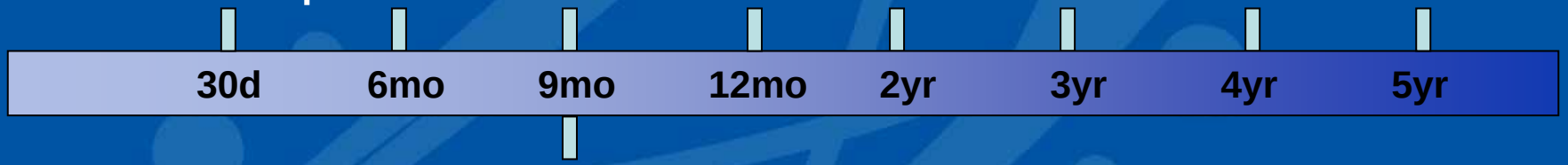
Stent Diameters	Stent Lengths
2.5 mm	8, 13, 18, 23, 28 mm
3.0 mm	8, 13, 18, 23, 33 mm
3.5 mm	8, 13, 18, 23, 33 mm

1670 subjects
~ 75 sites
USA and Canada

ZoMaxx™ Stent
N=835

TAXUS™ Stent
N=835

Clinical follow-up



Radiographic follow-up **QCA/IVUS**

Primary endpoint:	**Non-inferiority to TAXUS using 9-mo ischemia driven target vessel revascularization (TVR)**
Secondary endpoint:	**In-segment late loss at 9 mo. (QCA)**
Additional Analyses:	**Binary restenosis, MACE, TLR, TVR, in-stent late loss, neointimal volume, clinical outcomes by vessel diameter and lesion lengths**
Medications:	**Clopidogrel 75 mg QD for 6 months, ASA 325 mg QD for at least 12 months**

Presented by A. Yeung, TCT 2004, Washington, DC

ZOMAXX I and II Core labs

Data Center

- Harvard Clinical Research Institute, Boston

QCA

- Brigham and Women's, Boston

IVUS

- Stanford Interventional Cardiology, Palo Alto

ECG

- Harvard Clinical Research Institute, Boston

TriMaxx and ZoMaxx Regulatory Status

- The TriMaxx™ Coronary Stent is currently CE Mark approved
- The ZoMaxx™ Drug-Eluting Coronary Stent is not approved for sale
  - The ZOMAXX I & II clinical trial is currently enrolling patients