

TCT Asia 2006

**Current Data Indicates No Clinically
Relevant Differences Between
CYPHER and TAXUS!**

Eberhard Grube MD
FACC, FSCAI

Heart Center Siegburg, Siegburg, Germany
Stanford University, School of Medicine, CA, USA

TCT Asia 2006

Bah Humbug!

Current data indicate no clinically
relevant differences between CYPHER
and TAXUS!

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Heart Center Siegburg, Siegburg, Germany
Stanford University, School of Medicine, CA, USA

DES in 2006

Safety and Efficacy Proven!!

Drug

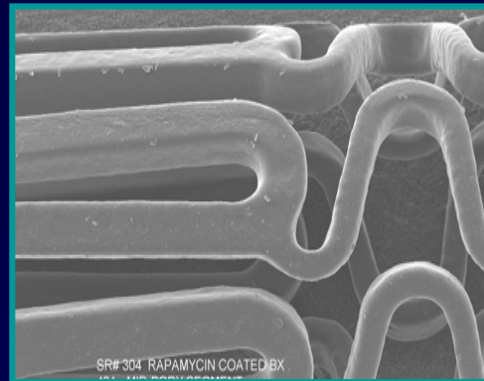
Polymer

Stent

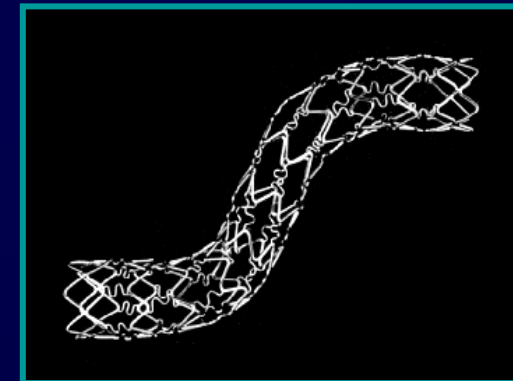
Cypher



Sirolimus

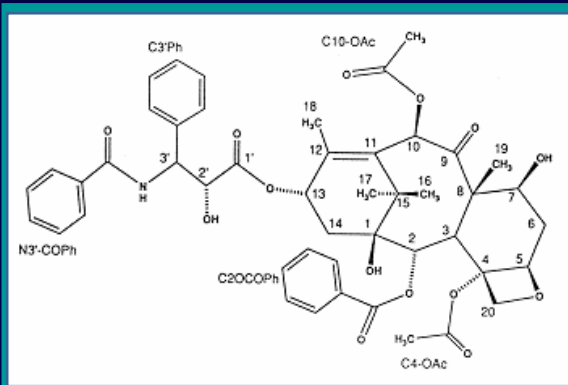


PEVA + PBMA blend

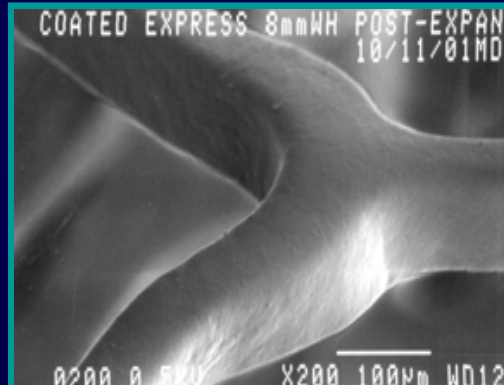


BX Velocity

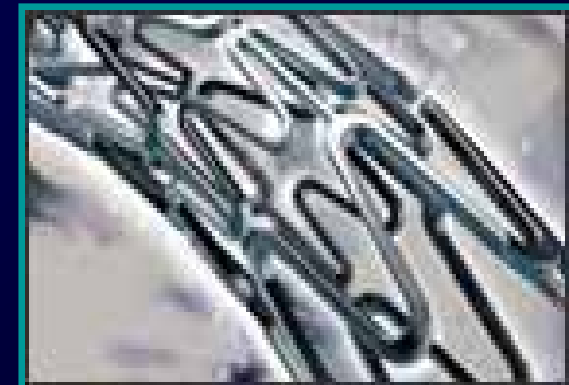
TAXUS



Paclitaxel



Polyolefin derivative



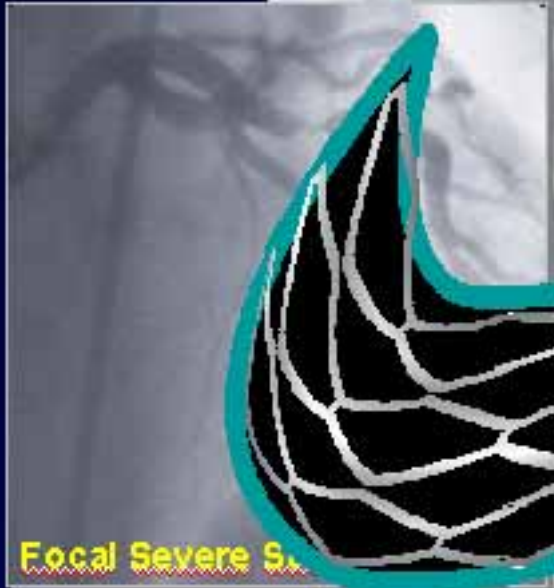
Express²



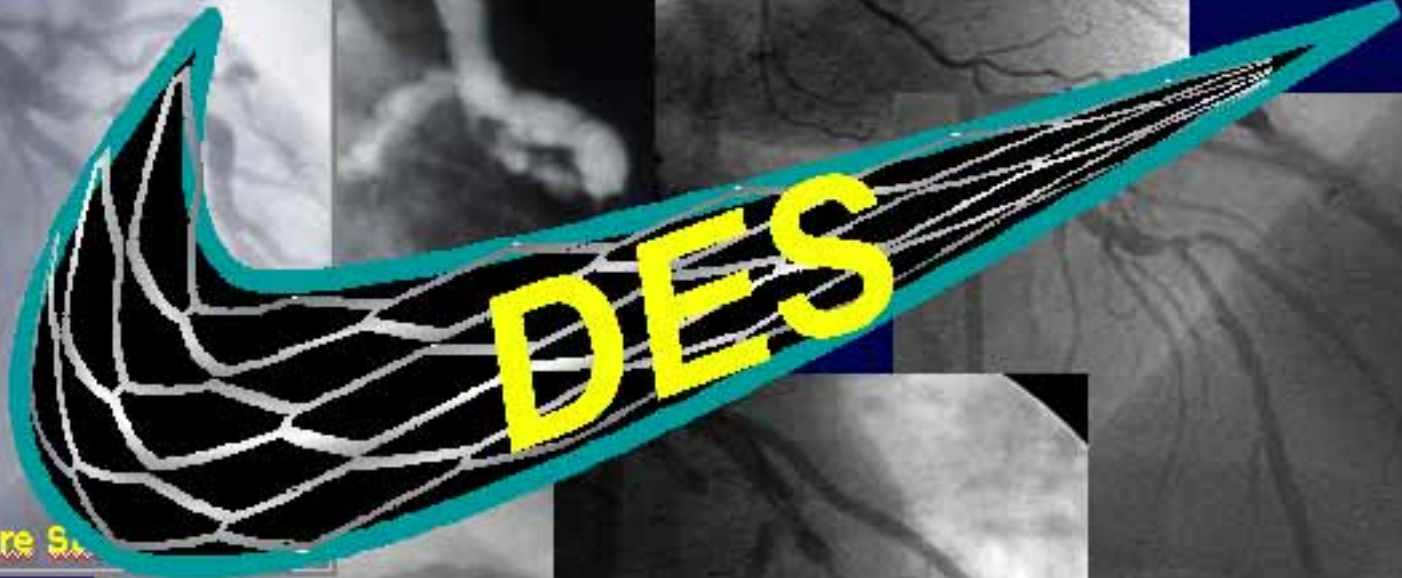
SVG



In-stent



Focal Severe Stenosis



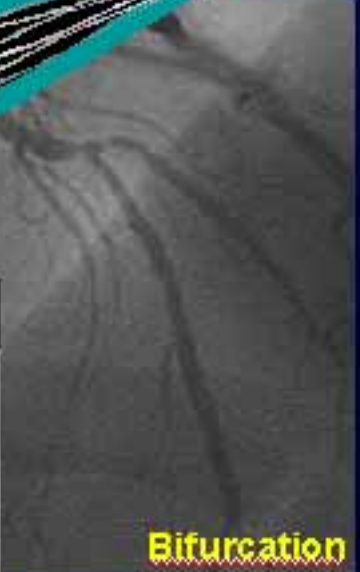
DES



Focal Mild Stenosis



Diffuse



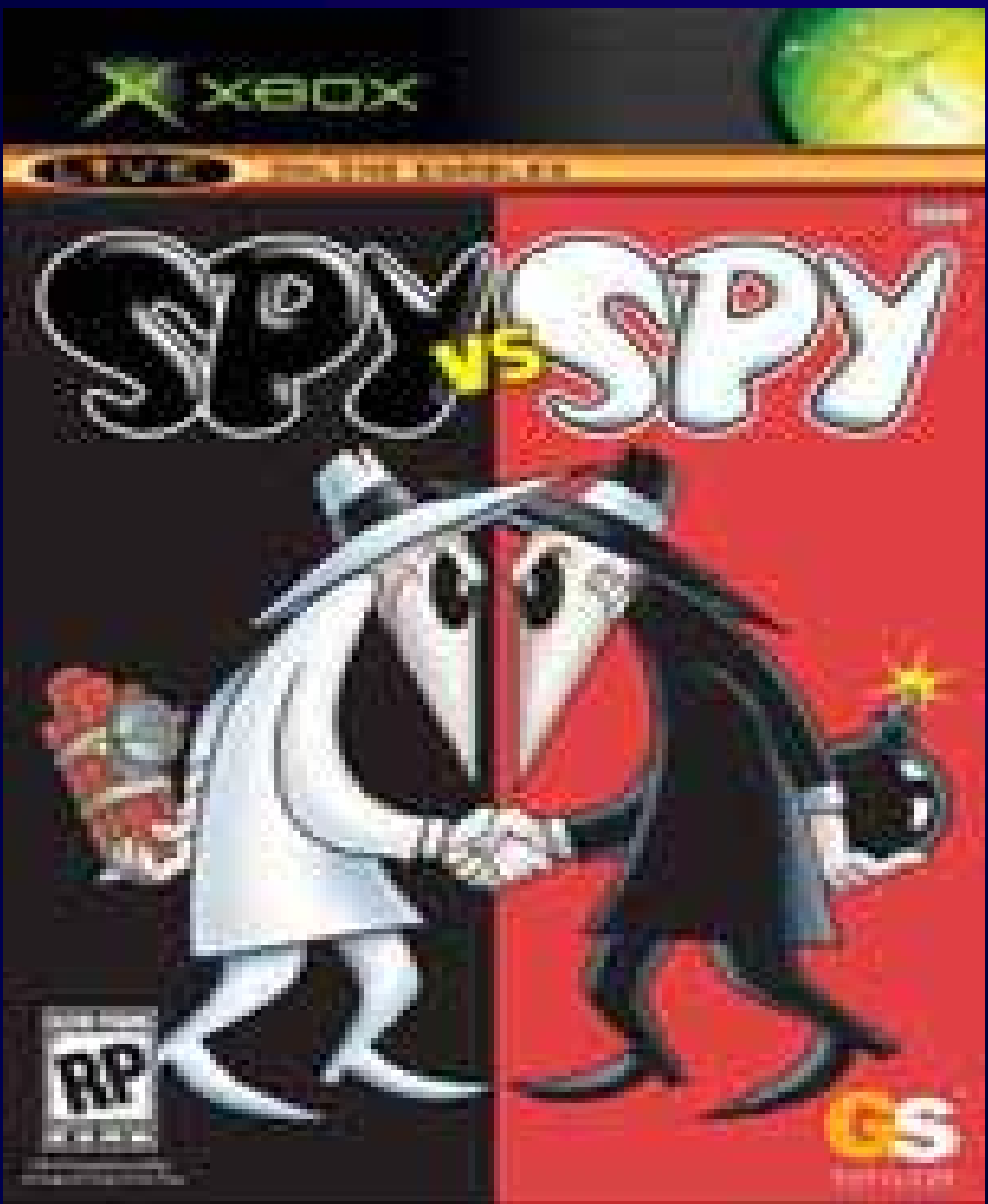
Bifurcation

CYPHER



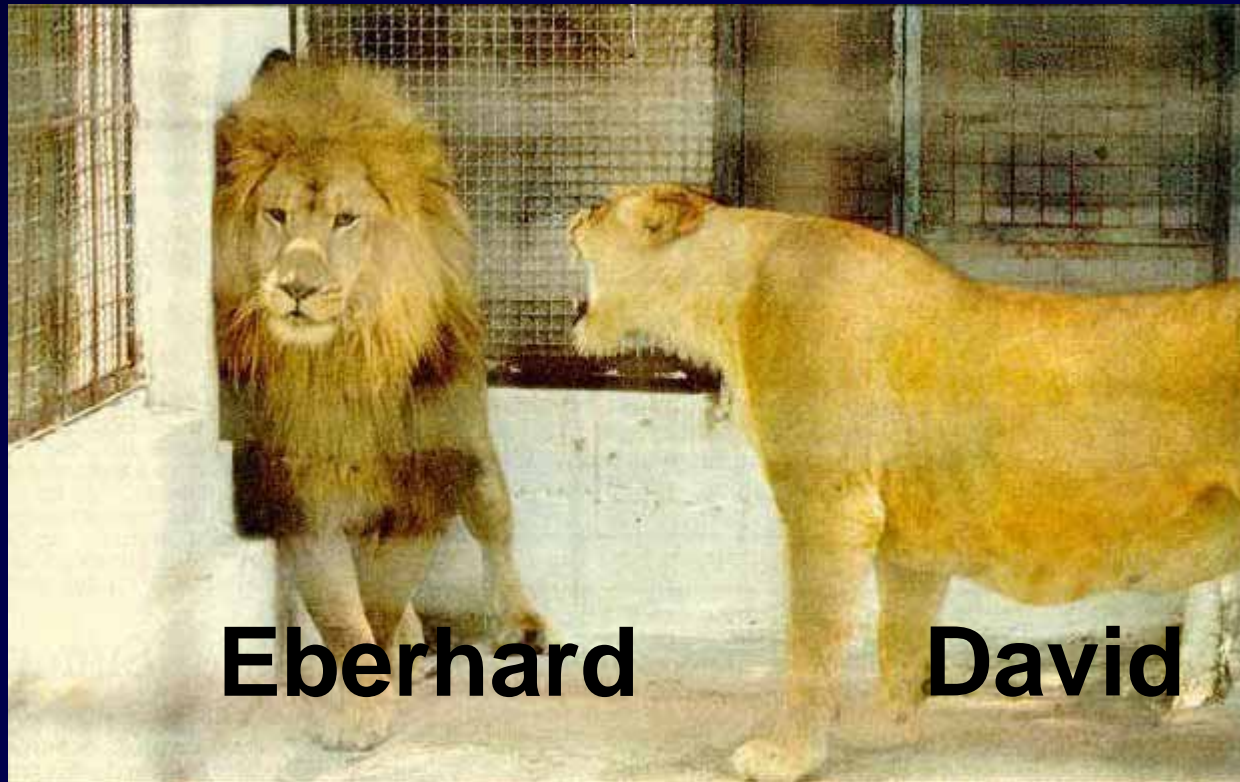
TAXUS

CYPHER EVANGELISTS



TAXUS DISCIPLES

Debates can get a bit out of hand....



Eberhard

David

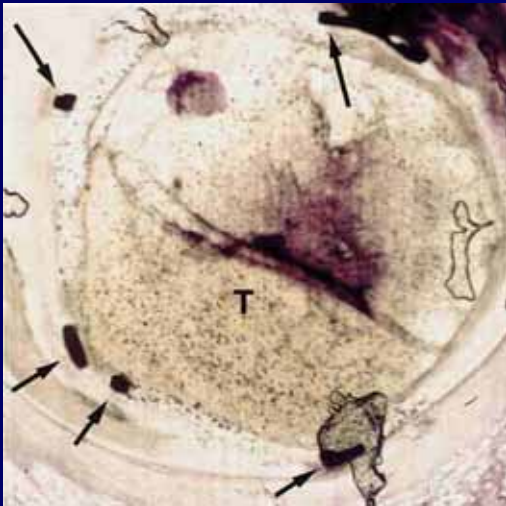
*Usually the most passionate, funniest
(and loudest) debater wins!*

Drug Eluting Stents on the European Market

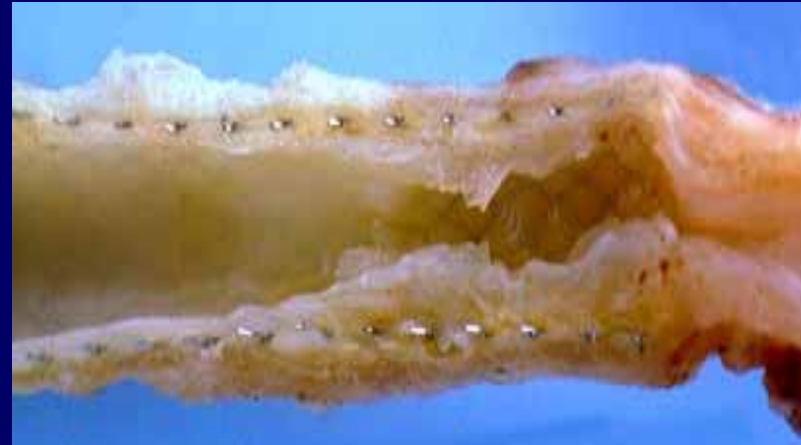


Are there clinical differences in terms of

Safety

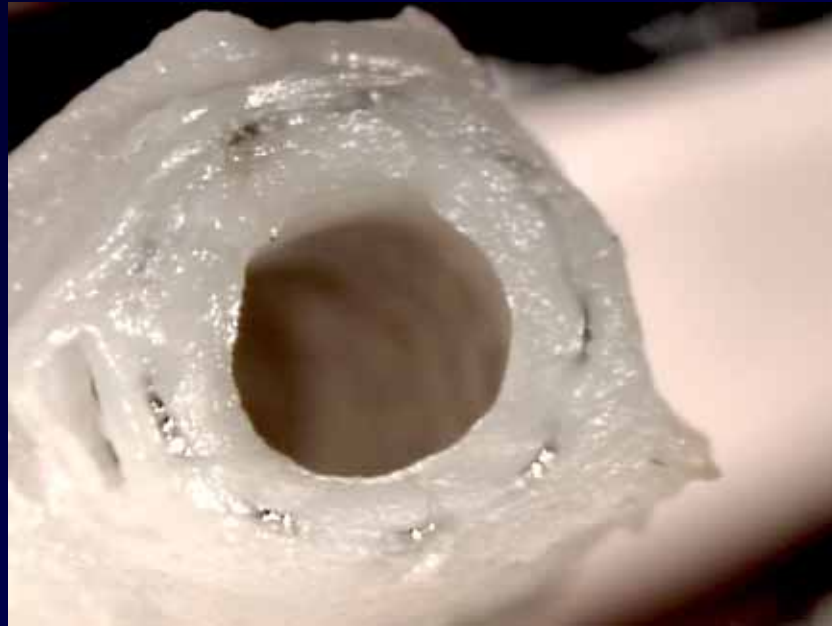


Efficacy

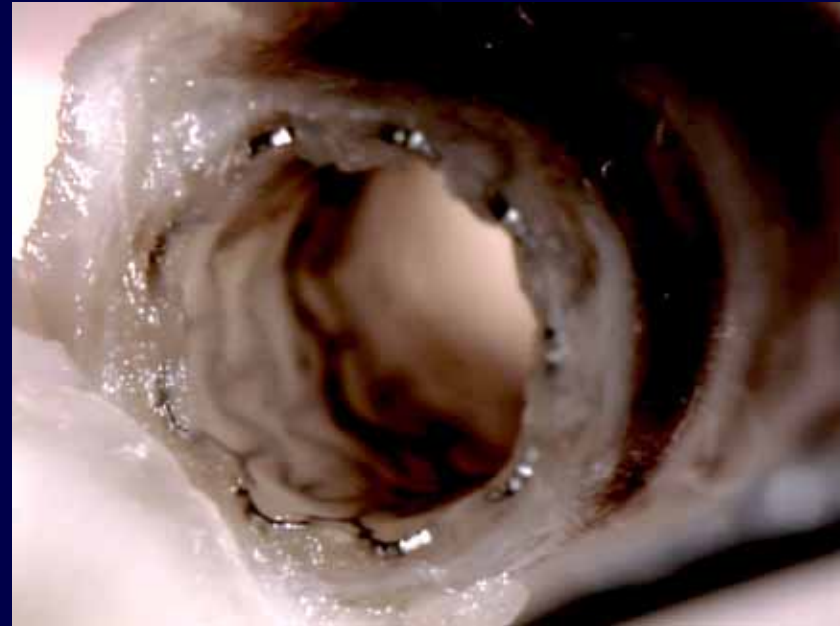


***Are CYPHER and TAXUS
Equally Effective?***

What is Efficacy?



BMS



DES

...to avoid intimal hyperplasia

What is Efficacy?

Intimal Hyperplasia



Angiographic Surrogate
Late Lumen Loss

This is the purest surrogate



Clinical Surrogate
Target Lesion Revascularization

This matters the most for the patient

SIRIUS Results

TLR: Subset Summary

| | Sirolimus | Control | | P-value | # events prevented per 1,000 patients |
|--------------------------------|-----------|---------|--|---------|---------------------------------------|
| Overall | 4.1 | 16.6 | | 0.0001 | 124 |
| Male | 4.4 | 16.6 | | 0.0001 | 122 |
| Female | 3.4 | 16.5 | | 0.0007 | 130 |
| Diabetes | 6.9 | 22.3 | | 0.0006 | 154 |
| No Diabetes | 3.2 | 14.3 | | 0.0001 | 111 |
| LAD | 5.1 | 19.8 | | 0.0001 | 147 |
| Non-LAD | 3.4 | 14.3 | | 0.0001 | 109 |
| Small Vessel (<2.75) | 6.3 | 18.7 | | 0.0001 | 125 |
| Large Vessel | 1.9 | 14.8 | | 0.0001 | 128 |
| Short Lesion | 3.2 | 16.1 | | 0.0001 | 129 |
| Long Lesion (>13.5) | 5.2 | 17.4 | | 0.0001 | 122 |
| Overlap | 4.5 | 17.7 | | 0.0003 | 131 |
| No Overlap | 3.9 | 16.1 | | 0.0001 | 121 |

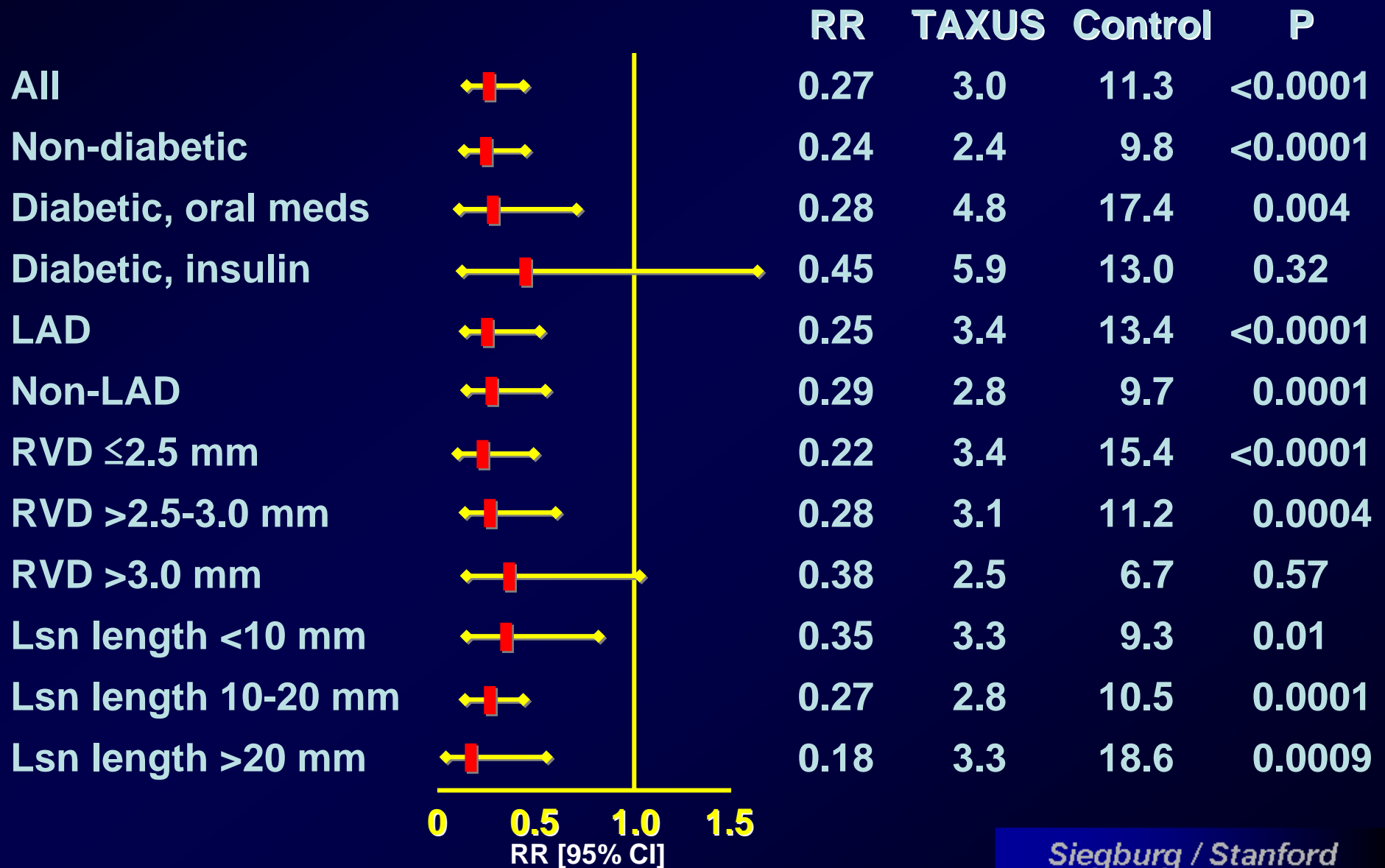
Hazards Ratio 95% CI 0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 0.9 0.8 0.7

Sirolimus better

Siegburg / Stanford

TAXUS IV Results

TLR: Subset Summary



CYPHER: Long-term results



Dante
Pazzanese

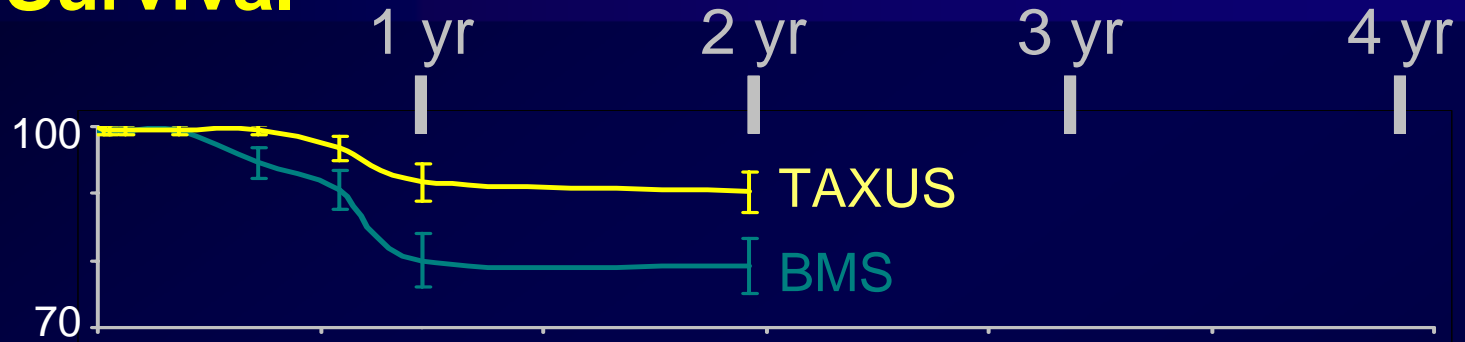
FIM Trial: 4-Year Event Free Survival (Death, MI, CABG, Re-PCI)



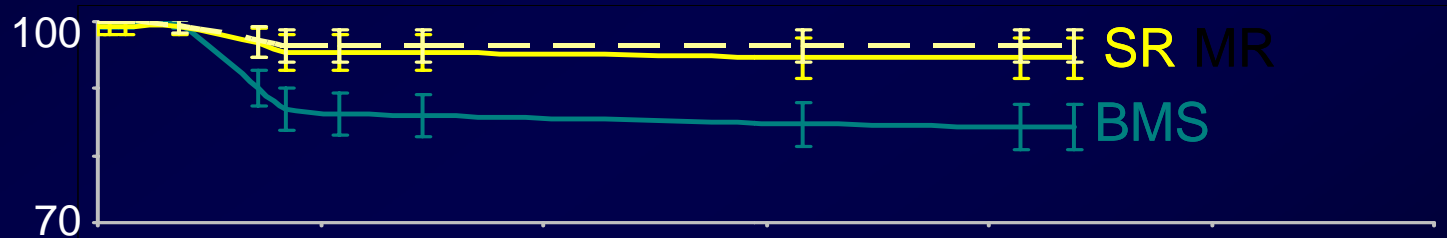
TAXUS: Long-term Results

Event-free Survival

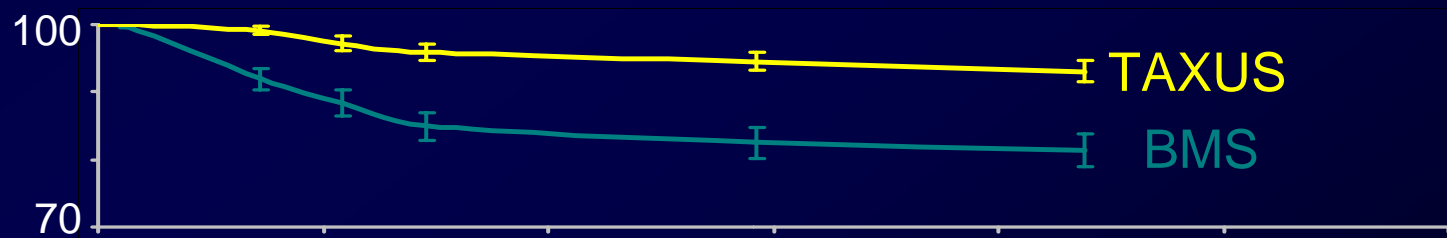
TAXUS VI



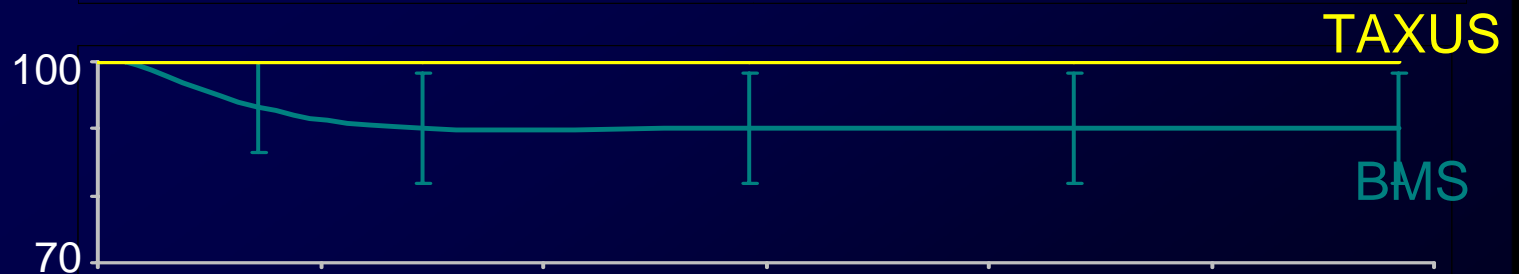
TAXUS II



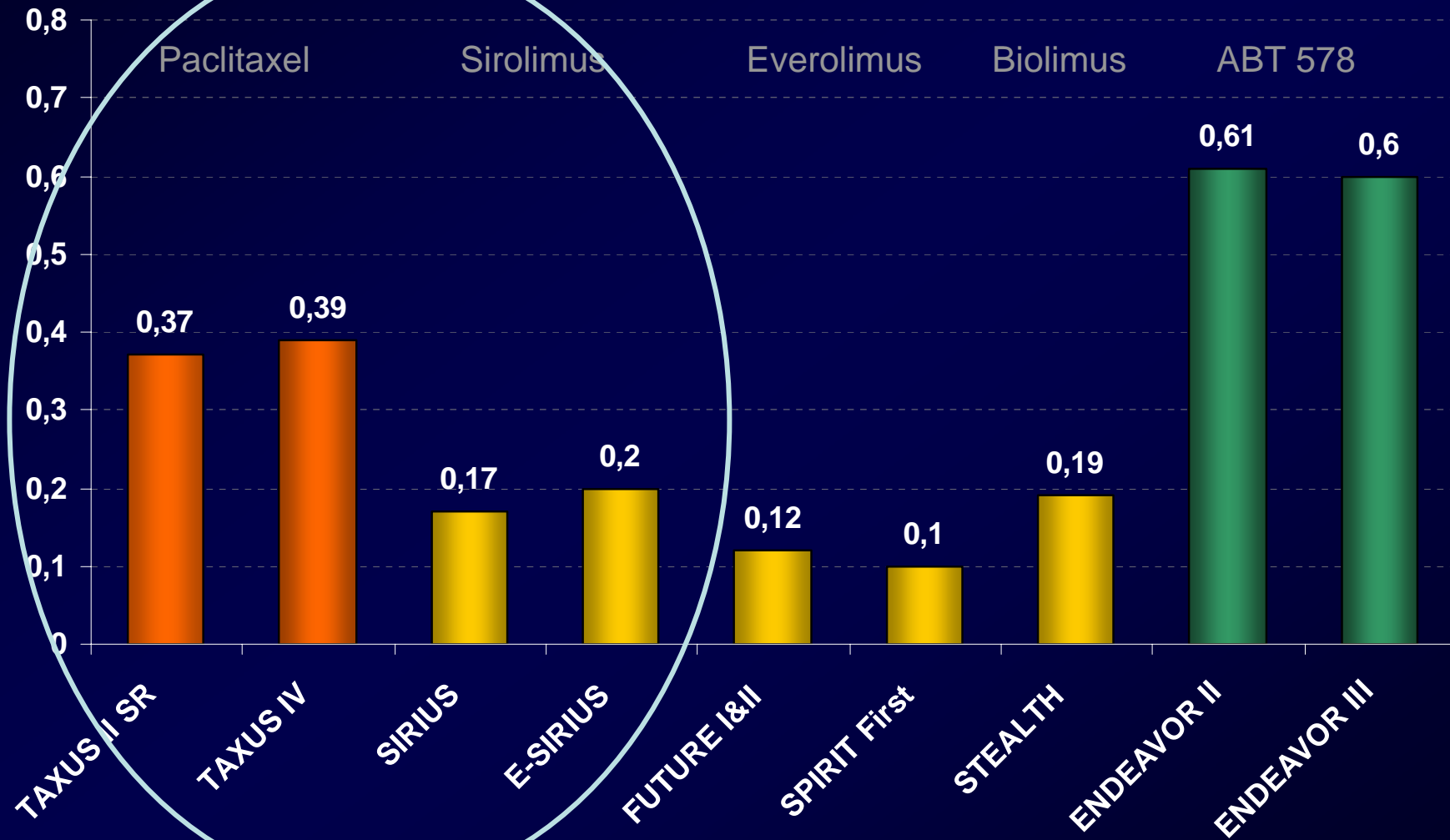
TAXUS IV



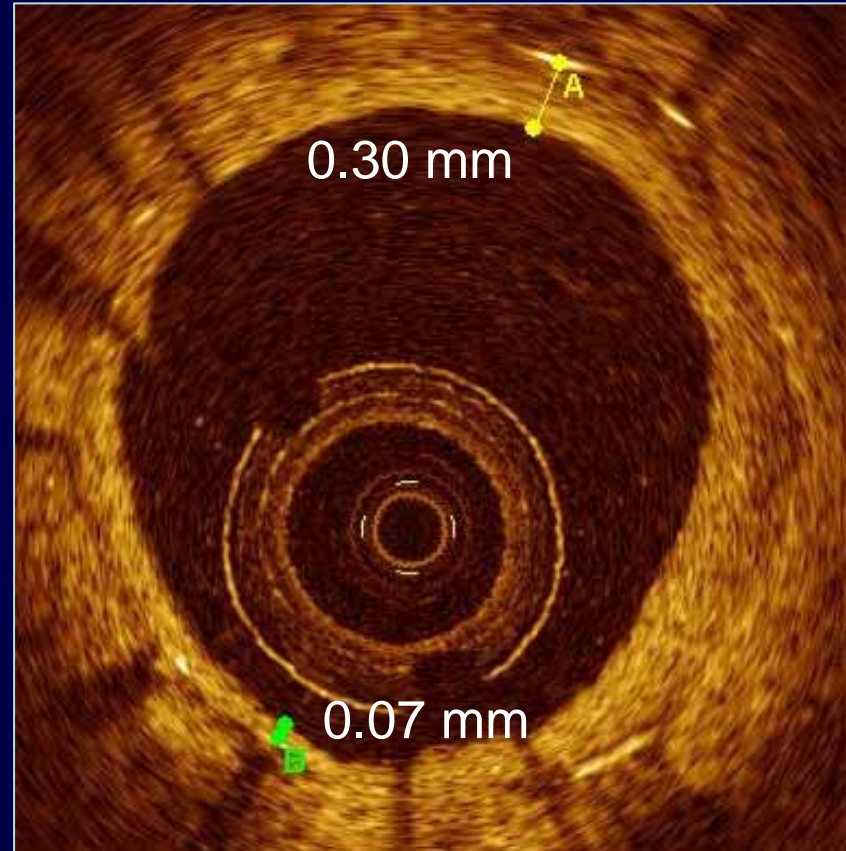
TAXUS I



Comparison In-stent Late Loss

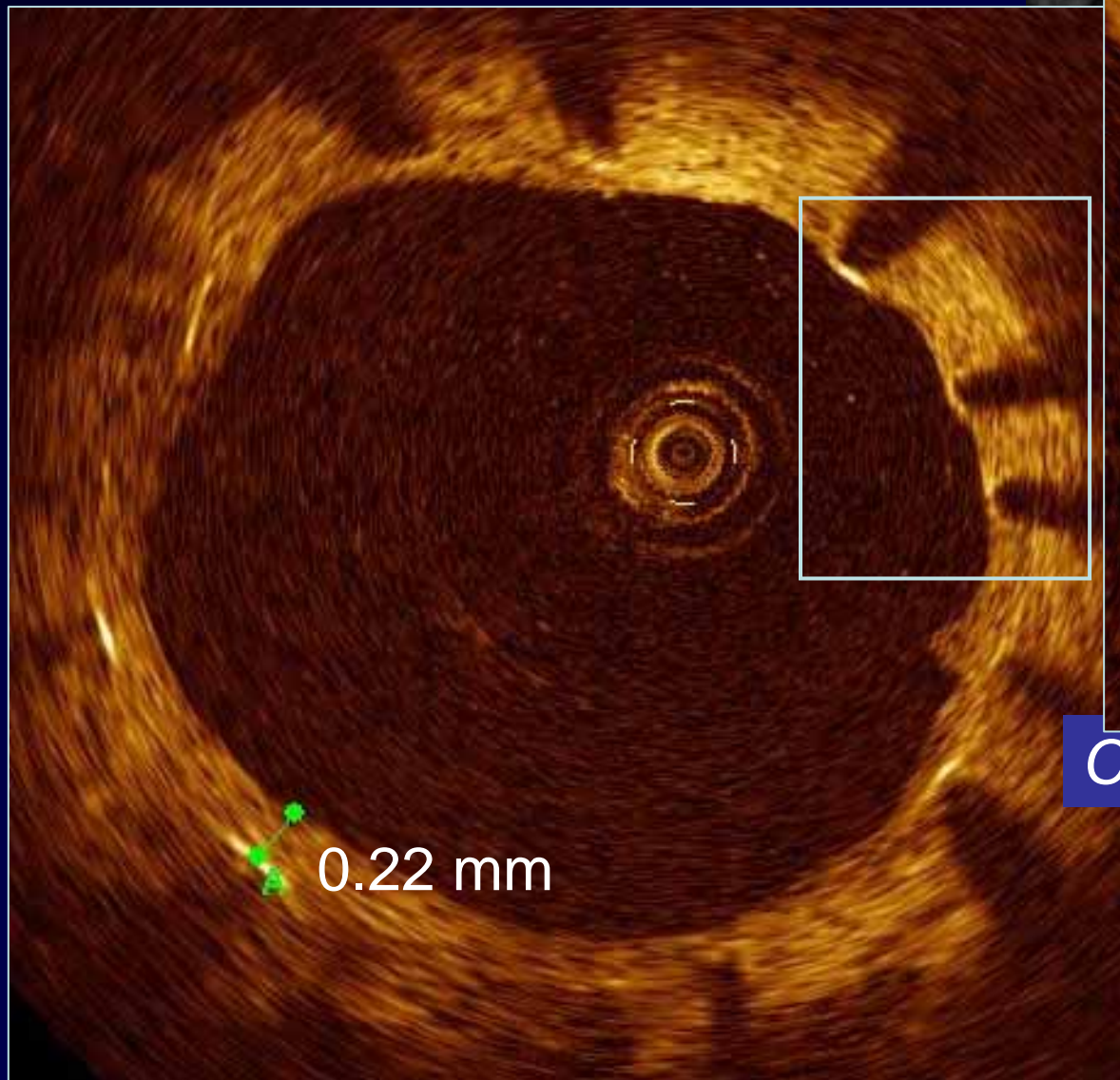


OCT in Taxus Follow-up



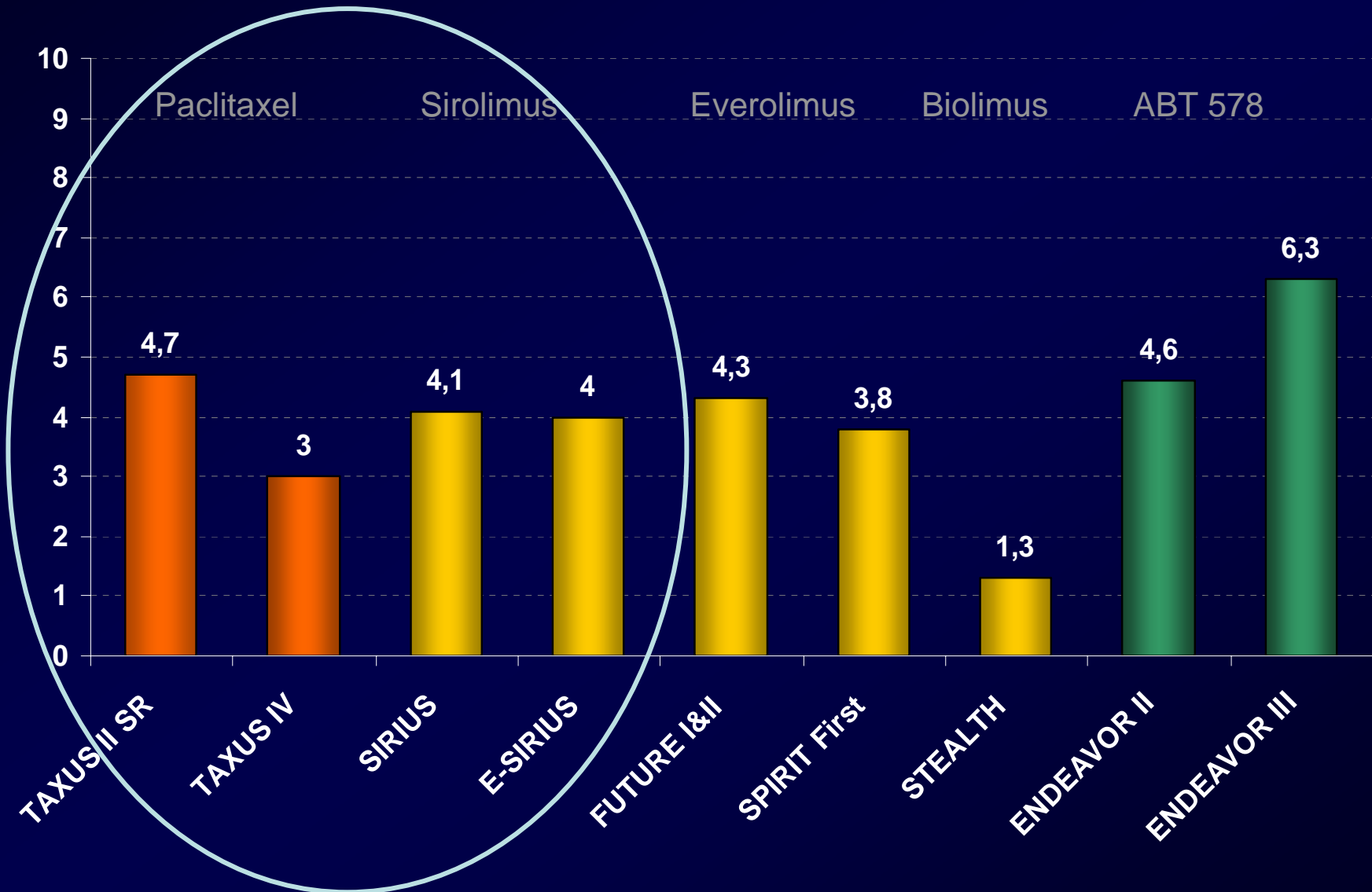
LCX - 16 mths follow-up

OCT in CYPHER Follow-up

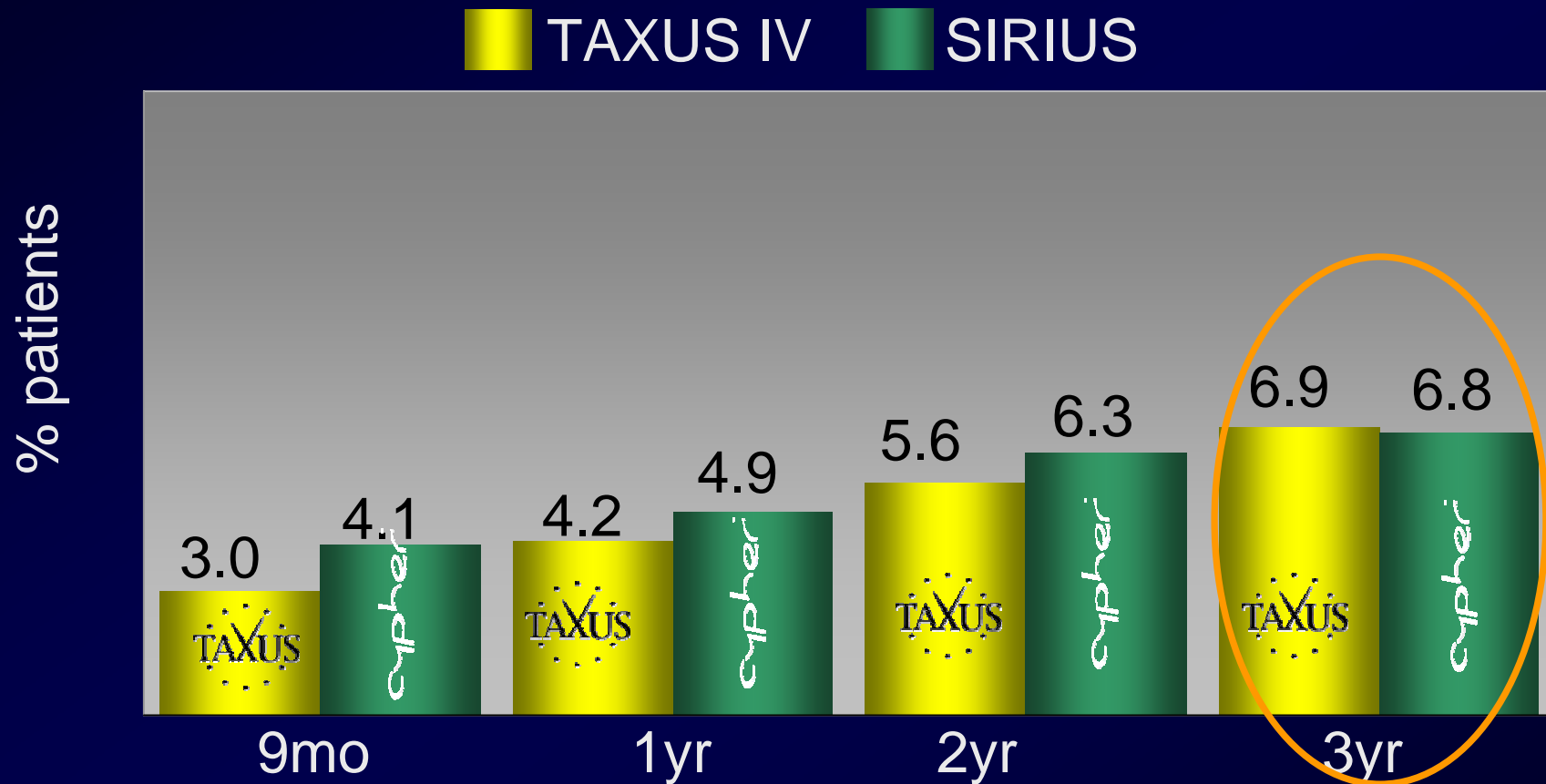


Cypher 10 mths follow-up

Comparison Target Lesion Revascularization



Compare TLR Rates in Pivotal Trials



SIRIUS & TAXUS IV equal at 3 years

Direct Comparison of Cypher and TAXUS “Head to Head” Trials

Journal of the American College of Cardiology
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EXPRESS PUBLICATIONS

A Prospective Randomized Comparison
Between Paclitaxel and Sirolimus Stents
in the Real World of Interventional Cardiology

Comparison of Short- (One Month) and Long- (Twelve Months) Term
of Sirolimus- Versus Paclitaxel-Eluting Stents in 293 Consecutive Patients
Diabetes Mellitus (from the RESEARCH and T-SEARCH Registries)

Andrew T. L. Ong, MBBS, Jiro Aoki, MD, Carlos A. G. van Mieghem, MD,
Gaston A. Rodriguez Granillo, MD, Marco Valgimigli, MD, PhD,
Karel Sonnenschein, Evelyn Regar, MD, PhD, Willem J. van der Giessen,
Peter P. T. de Jaegere, MD, PhD, Georgios Sianos, MD, PhD,
Eugene P. McFadden, MBChB, MD, Pim J. de Feyter, MD, PhD,
Ron T. van Domburg, PhD, and Patrick W. Serruys, MD, PhD, FACC

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 18, 2005

Paclitaxel-Eluting or Sirolimus-Eluting Stents
Prevent Restenosis in Diabetic Patients

Dibra, Alban; Kastrati, Adnan; Mehilli, Julinda; Pache, Jurgen; Schuhlen
Nicolas; Ulm, Kurt; Wessely, Rainer; Dirschinger, Josef; Serruys, Patrick W.

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 18, 2005 VOL. 353 NO. 7

Sirolimus-Eluting and Paclitaxel-Eluting Stents
for Coronary Revascularization

Windecker, Stephan; Remondino, Andrea; Eberli, Franz R.; Juni, Peter; Raber, Lorenz;
Wenaweser, Peter; Togni, Mario; Billinger, Michael; Tuller, David; Seiler, Christian; Roffi, Marco; Corti,
Roberto; Sutsch, Gabor; Maier, Willibald; Luscher, Thomas; Hess, Otto M.; Egger, Matthias; Meier, Bernhard

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ISSN 0735-1097/05/430.00
doi:10.1016/j.jacc.2004.09.079

Thirty-Day Incidence and Six-Month Clinical
Outcome of Thrombotic Stent Occlusion After
Bare-Metal, Sirolimus, or Paclitaxel Stent Implantation

Andrew T. L. Ong, MBBS, FRACP, Angela Hoye, MBChB, MRCP, Jiro Aoki, MD,
Carlos A. G. van Mieghem, MD, Gaston A. Rodriguez Granillo, MD, Karel Sonnenschein,
Evelyn Regar, MD, PhD, Eugene P. McFadden, MBChB, MD, FRCPI, FACC,
Georgios Sianos, MD, PhD, Willem J. van der Giessen, MD, PhD, Peter P. T. de Jaegere, MD, PhD,
Pim de Feyter, MD, PhD, FACC, Ron T. van Domburg, PhD, Patrick W. Serruys, MD, PhD, FACC
Rotterdam, The Netherlands

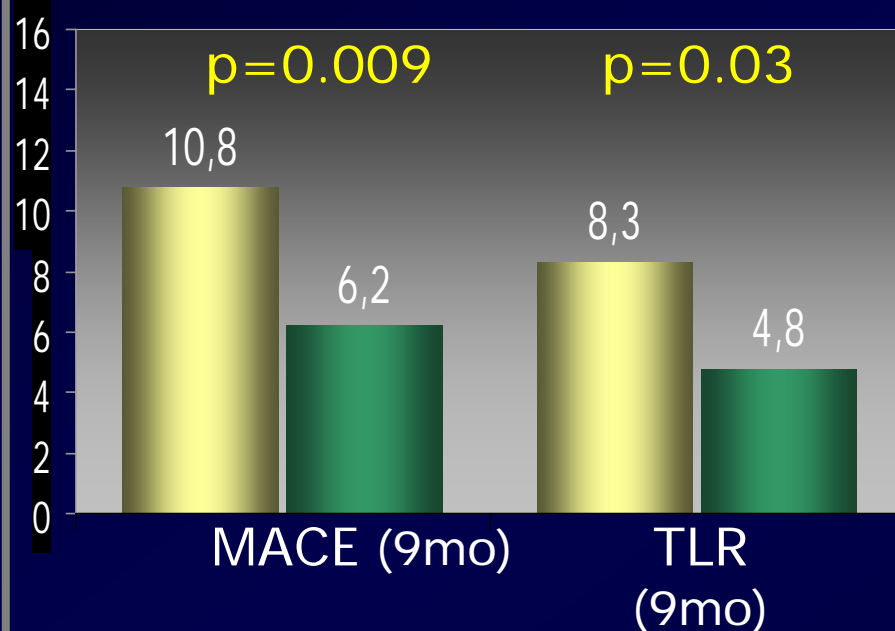
The DES Cypher vs. Taxus RCTs

- TAXi
- ISAR - Desire
- SIRTAX
- CORPAL
- ISAR – Diabetes
- REALITY
- Research, T-Search Diabetes

Head to Head Trials -TAXUS vs. CYHPER

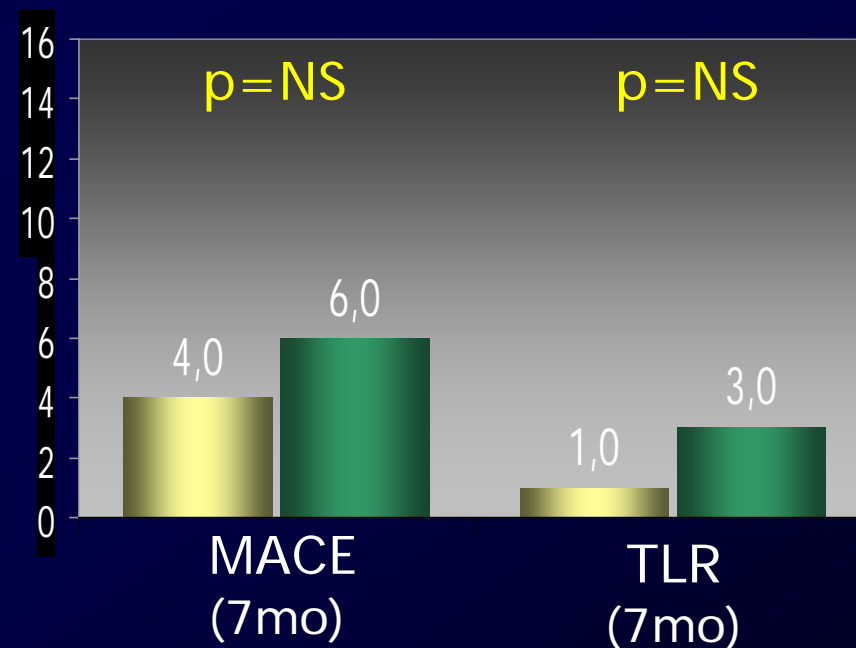
SIRTAX

■ TAXUS (509 pts) ■ CYPHER (503 pts)



TAXi

■ TAXUS (100 pts) ■ CYPHER (102 pts)



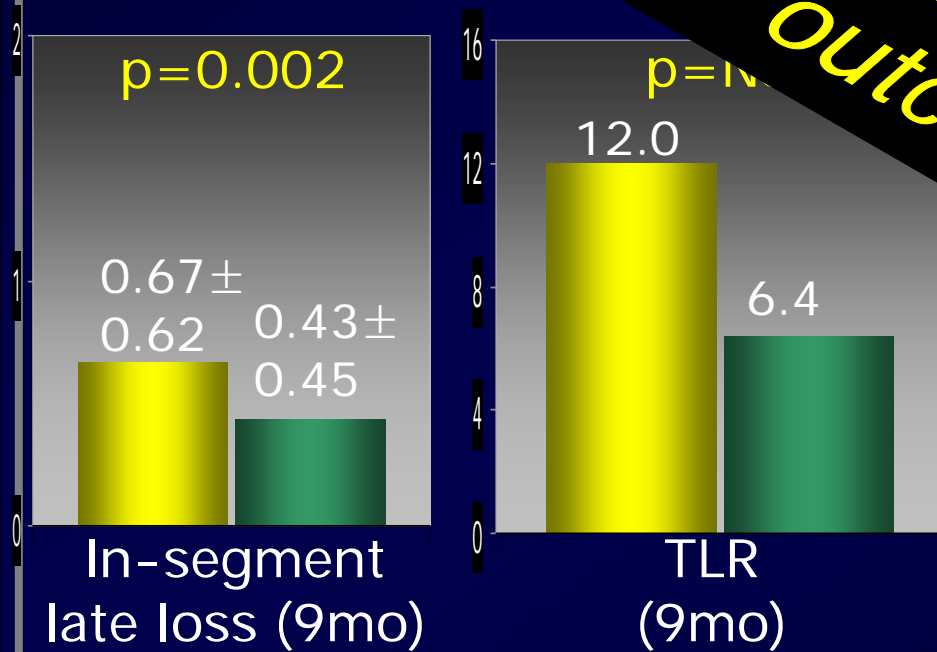
➔ *Contradictory study outcomes!*

Head to Head Trials-*TAXUS VS. CYPHER*

Complex lesions

ISAR-*Diabetes*

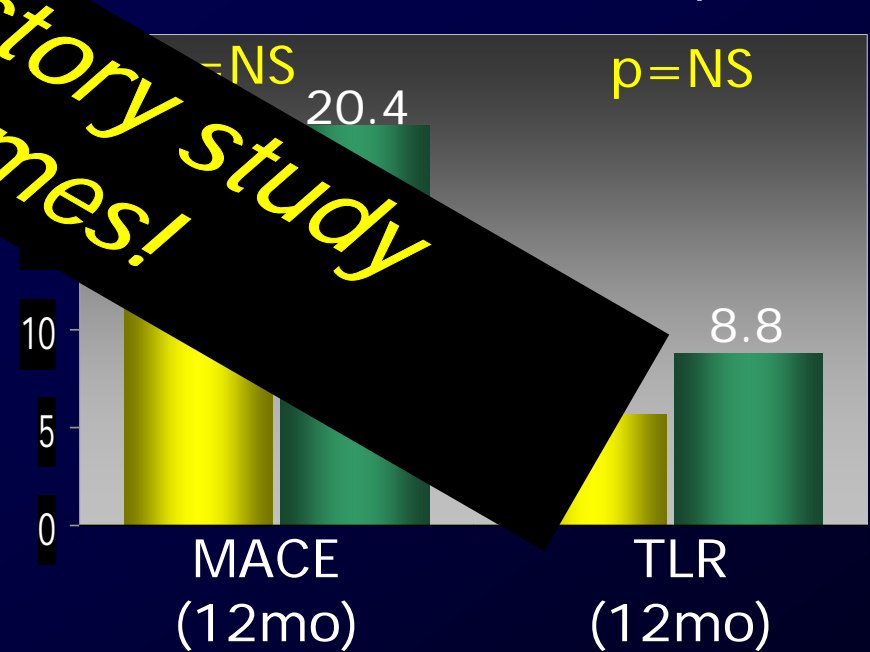
TAXUS
(125 pts)



Research/T-Search
Diabetes

TAXUS
(125 pts)

CYPHER
(148 pts)



Contradictory study outcomes!

***Why are we seeing these contrary outcomes
in head to head trials?***



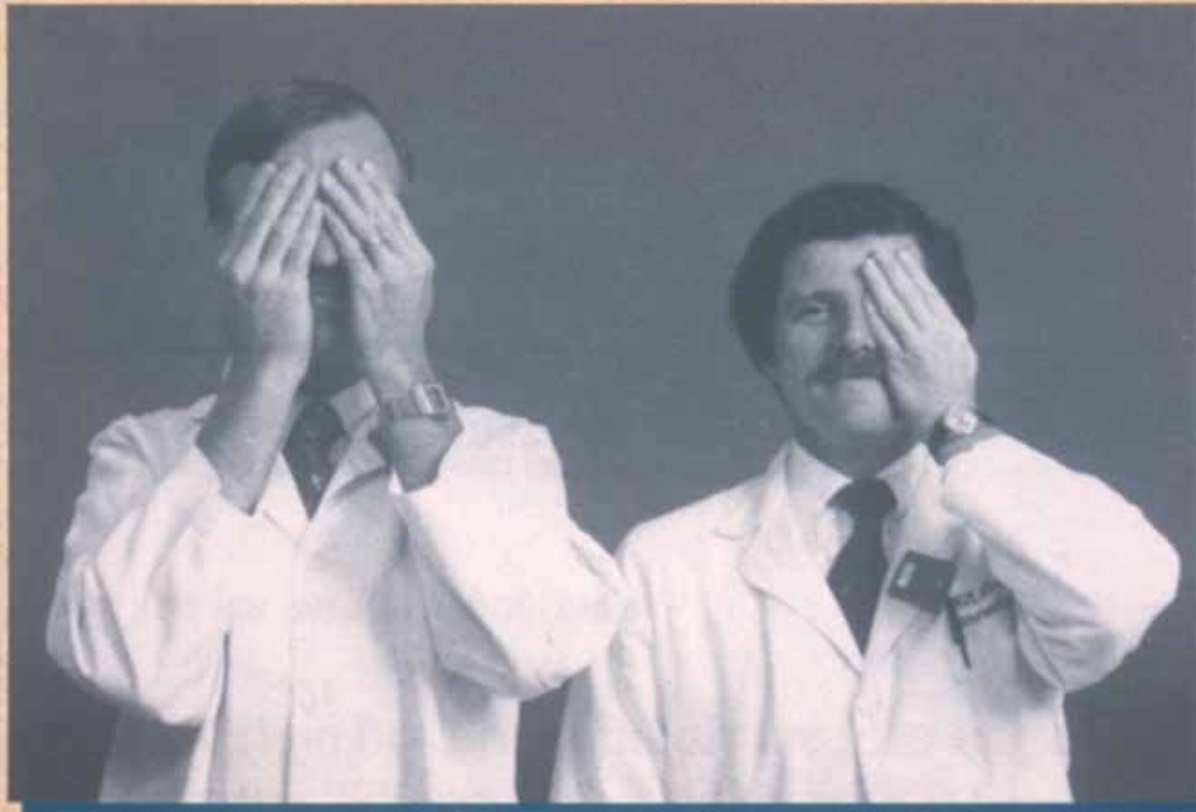
*Because if one looks closer
differences in trial design can be found...*

**Prospective, Multicenter, Blinded,
Placebo-Controlled,
Randomized Trials
represent the highest level of
evidence-based medicine.**

By far!

And remember....all DES RCTs
are single-blind studies

Single-Blind & Double Blind



Trying to be insightful about the DES RCT's...



Comparison of Head-to-Head Trials

| | SIRTAX | TAXi | RESAERCH/ T-SEARCH DIABETES | ISAR- DIABETE S | REALITY |
|------------------------------|--------|------|-----------------------------------|-----------------------|---------|
| Multi-center (>5 centers) | - | - | - | - | ✓ |
| Independent Core Lab | - | - | - | - | ✓ |
| Independent CEC | ✓ | - | ✓ | - | ✓ |

Windecker et al., NEJM 2005;353:653-63; Goy et al., JACC 2005;45:308-11; Kastrati et al., NEJM 2005; 353:663-70 ; Ong et al., AJC 2005; 358-62 ; REALITY, ACC 2005

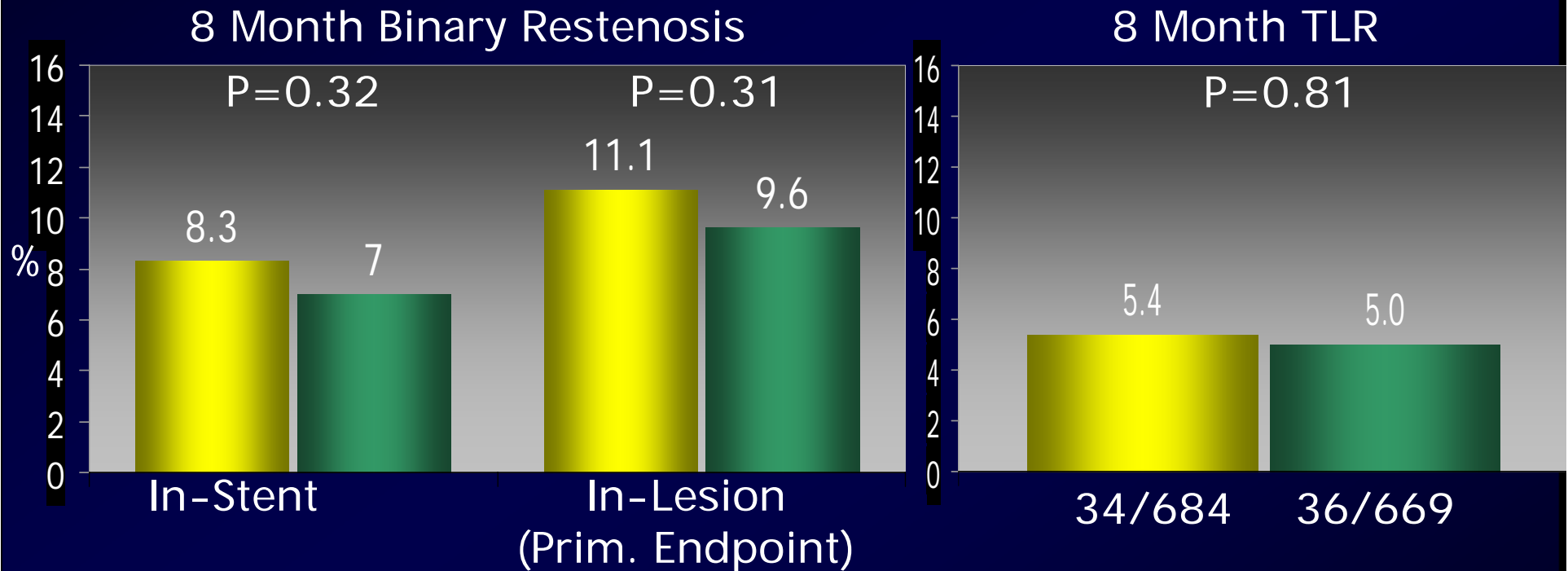
Siegburg / Stanford

Head to Head Trials

REALITY- Intention to Treat

■ TAXUS (669 pts; 941 lesions)

■ CYPHER (684 pts; 970 lesions)



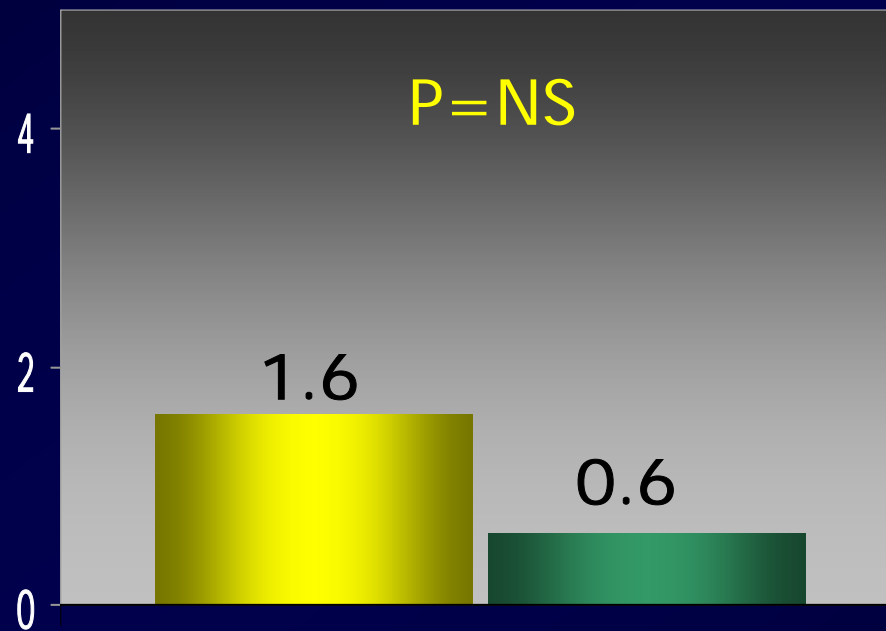
*Comparable efficacy results
between TAXUS and CYPHER*

***Are CYPHER and TAXUS
Equally Safe?***

Head to Head Trials

REALITY - Intention to Treat

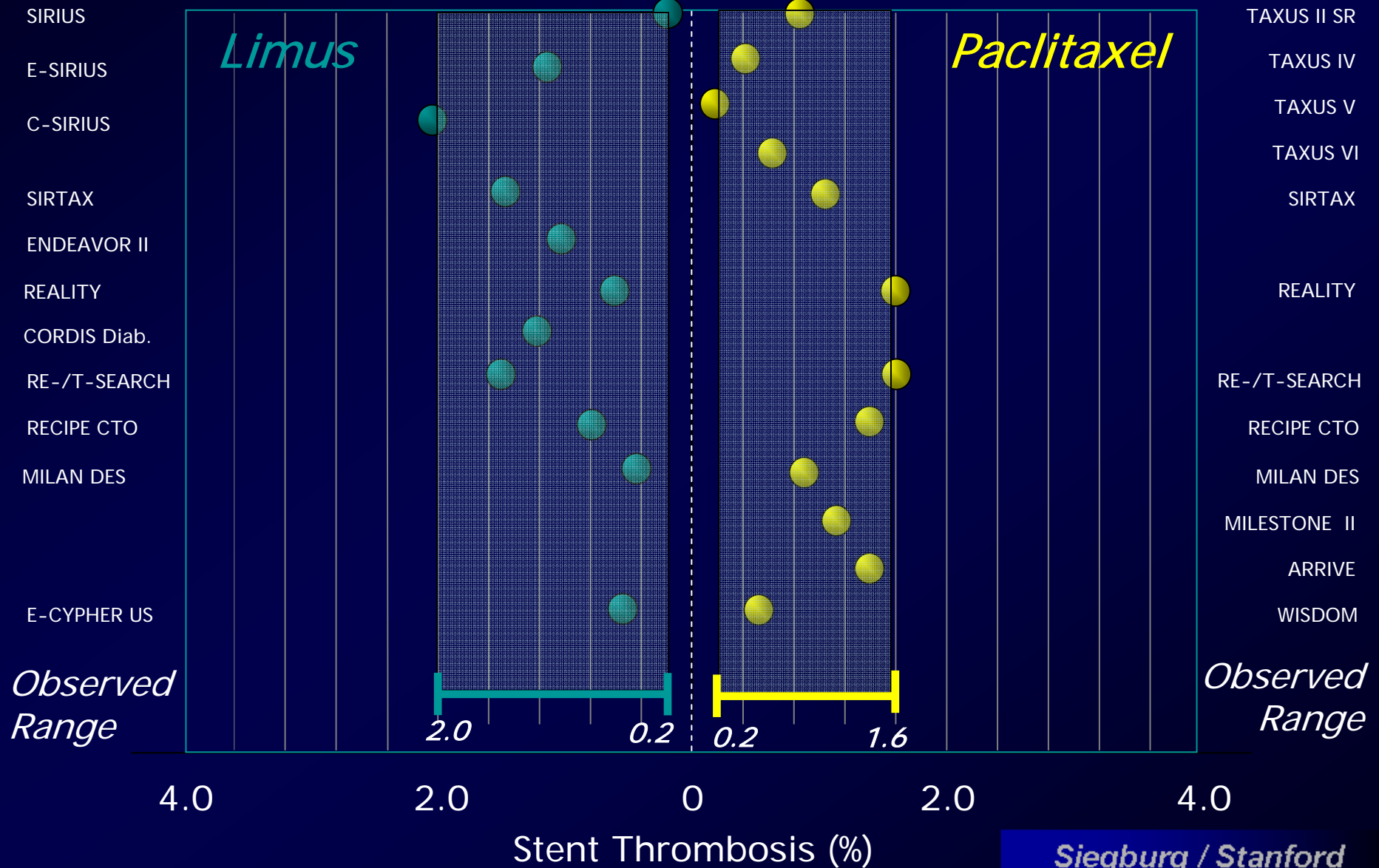
■ TAXUS (669 pts; 941 lesions) ■ CYPHER (684 pts; 970 lesions)



Stent Thrombosis (acute and subacute)

Stent Thrombosis: Up to 30 Days

Rates variable but similar across DES programs...



...despite different definitions of Stent Thrombosis

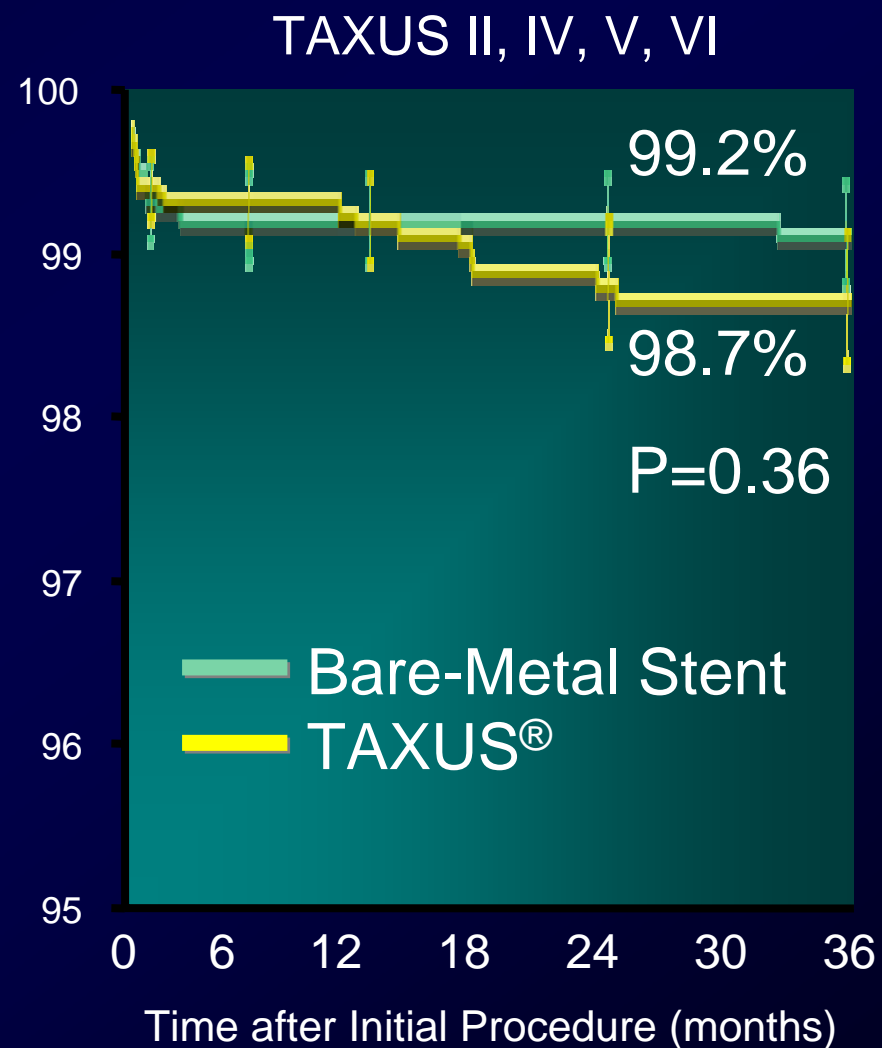
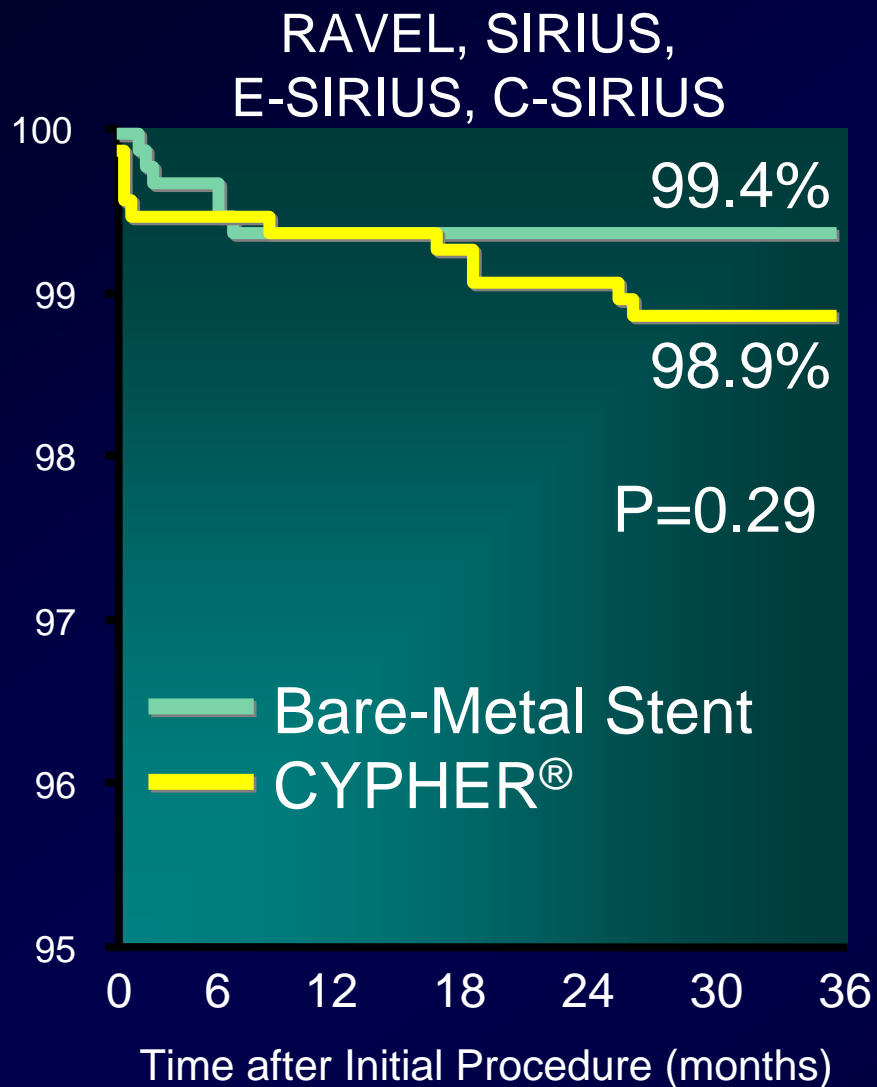
| | TAXUS ¹ | CYPHER ² | |
|----------------------------------|--------------------|---------------------|---------|
| | | ≤30d | >30d |
| Angiographic Confirmation | ✓ | +TLR or | ✓ |
| Sudden, unexplained death (≤30d) | ✓ | ✓ | - |
| Myocardial Infarction: | or | or | and |
| Q-Wave MI | ✓ or | ✓ | ✓ or |
| CK >2xULN | ✓ | | ✓ |

¹ From Stone *et al.*, *N Engl J Med* 2004 350: 221 and protocols for TAXUS IV and V clinical trials.

² From Cypher Instructions for Use and REALITY protocol

DES Safety

Comparison Stent Thrombosis Cypher – TAXUS - BMS

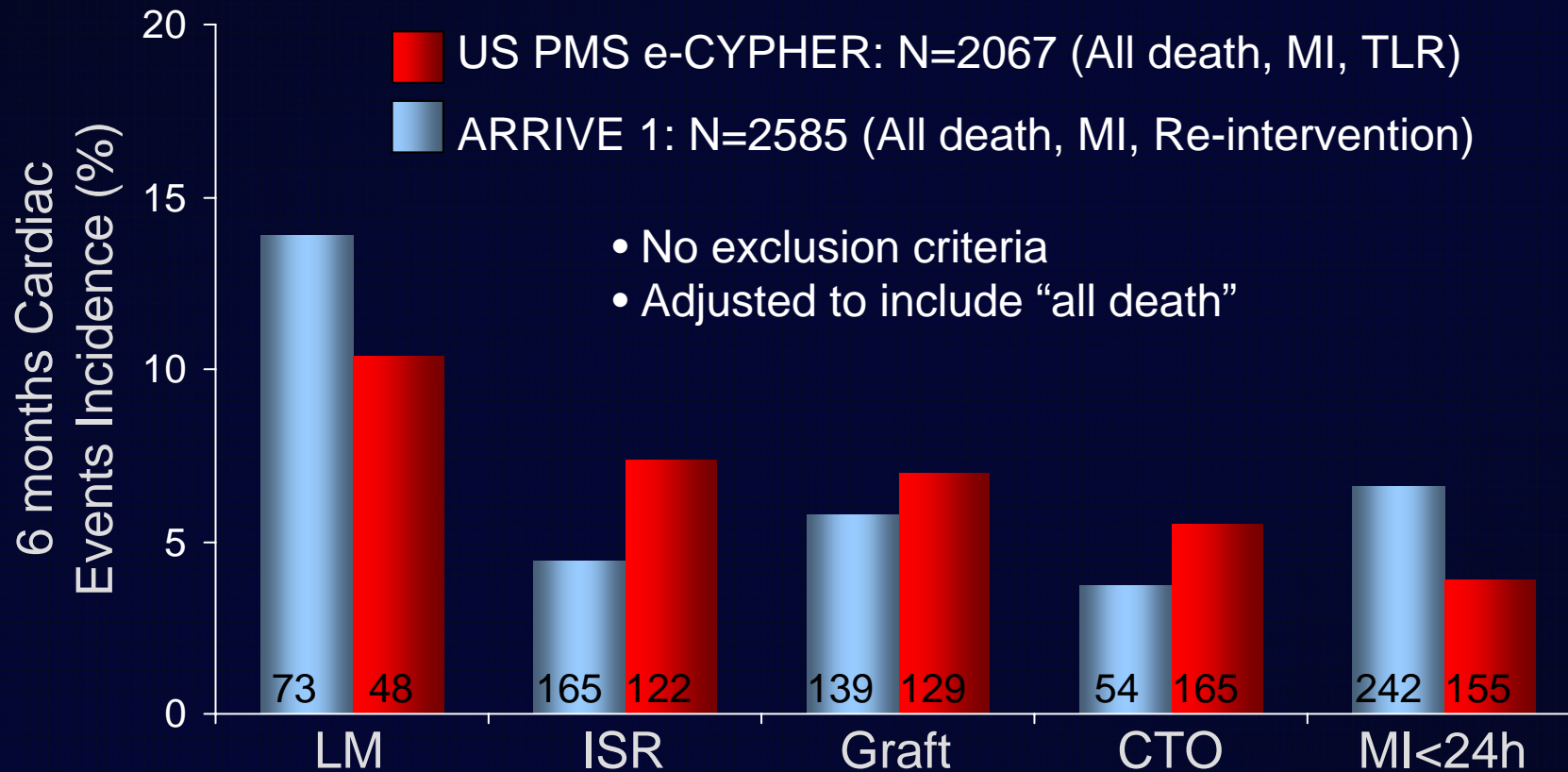


How does “real world” use of TAXUS and CYHPER Stent compare?



Results in Real World Higher Risk Subsets

US-PMS e-Cypher + ARRIVE 1 (2 Post Approval, FDA mandated DES Registries)



US PMS presented by P. Berger at ACC 2005
ARRIVE 1 presented by J. Lasala at EuroPCR 2005

Siegburg / Stanford

Conclusion

- Demonstration of comparable clinical outcomes for Limus and Paclitaxel Eluting Stents
- Comparable event rates between TAXUS and CYPHER in real world setting
- Comparable safety results for Limus and Paclitaxel Eluting Stents