Comparing First and Second Generation DES:

Latest Updates in DES Clinical Data

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The Cardiovascular Research Foundation

CARDIOVASCULAR RESEARCH FOUNDATION

COLUMBIA UNIVERSITY MEDICAL CENTER

Spirit

Disclosures

- Research support from Abbott Vascular and Boston Scientific

Drug-eluting Stents "First Gen US"

TAXUS

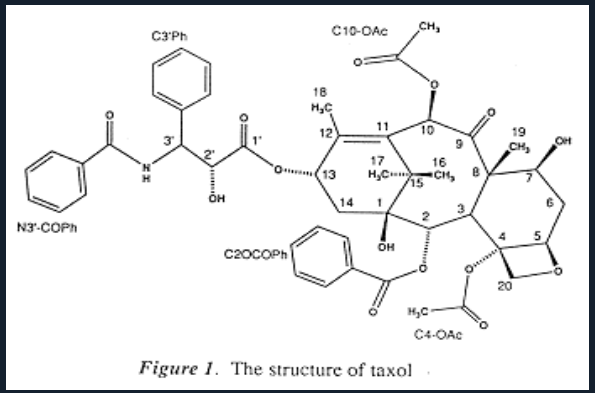
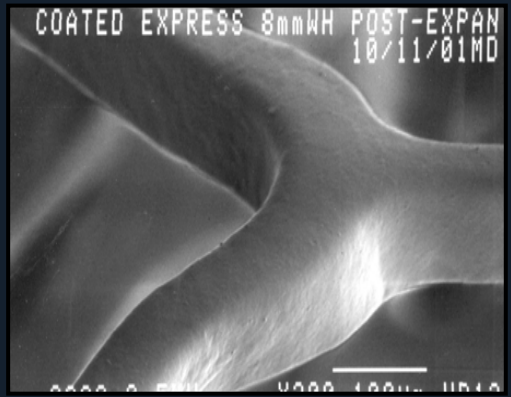


Figure 1. The structure of taxol

Paclitaxel

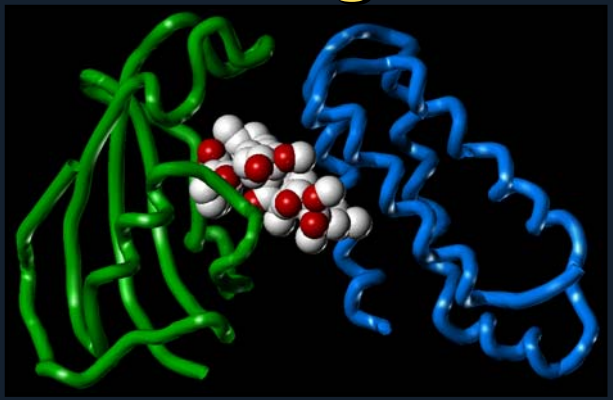


Polyolefin derivative

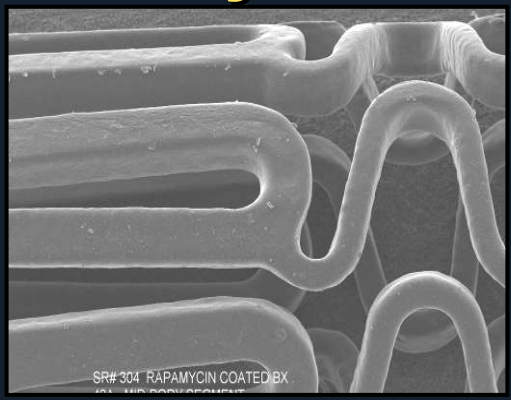
Expert[2]

Drug | **Polymer** | **Stent**

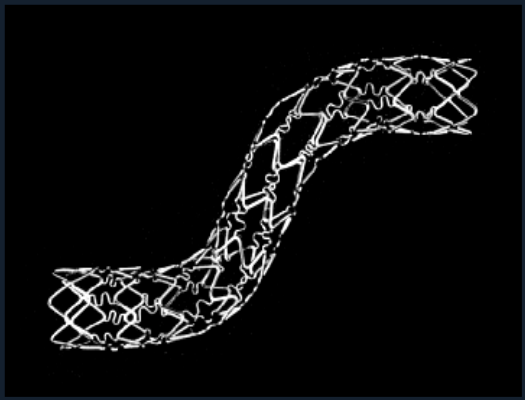
Cypher



Sirolimus



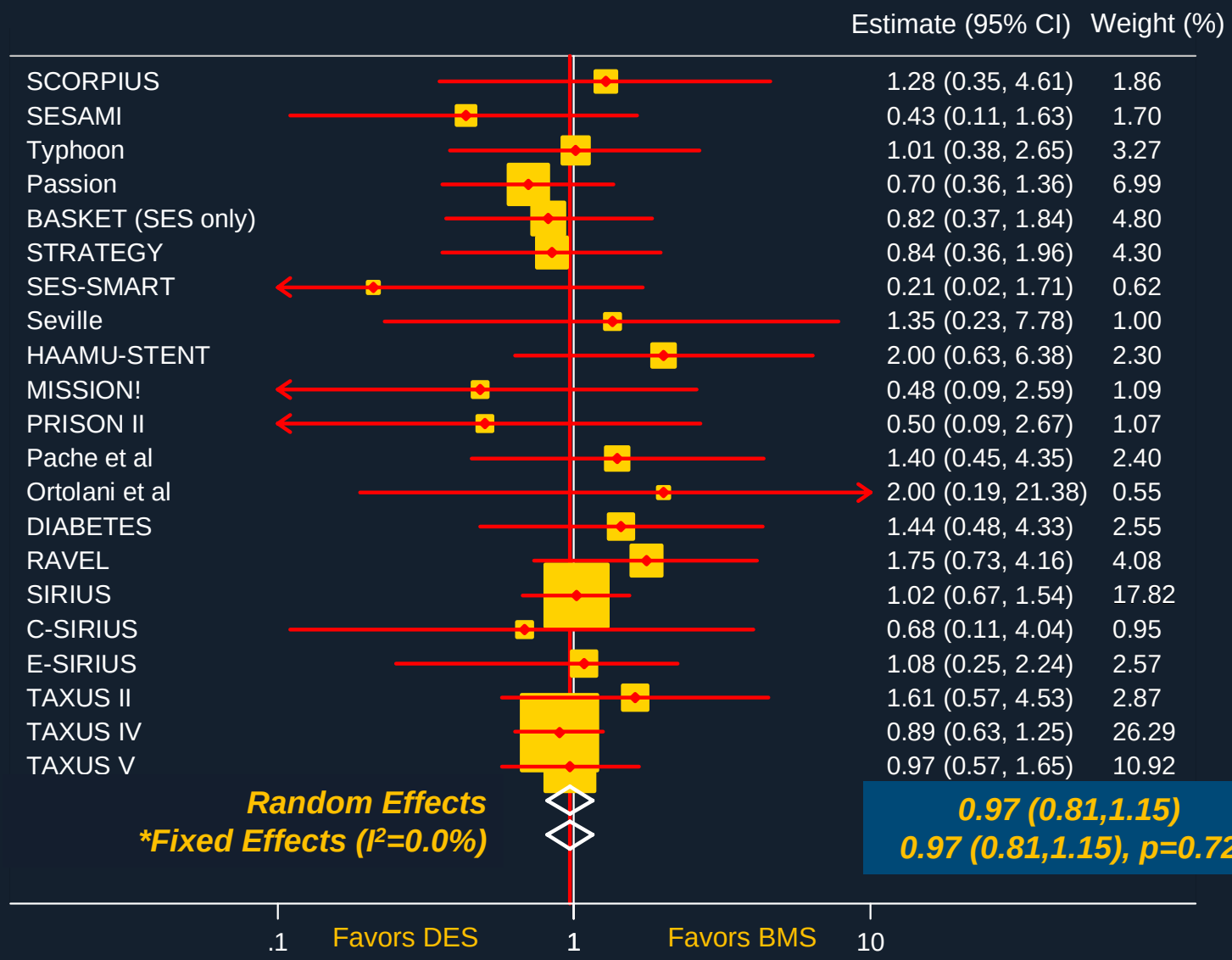
PEVA + PBMA blend



BX Velocity

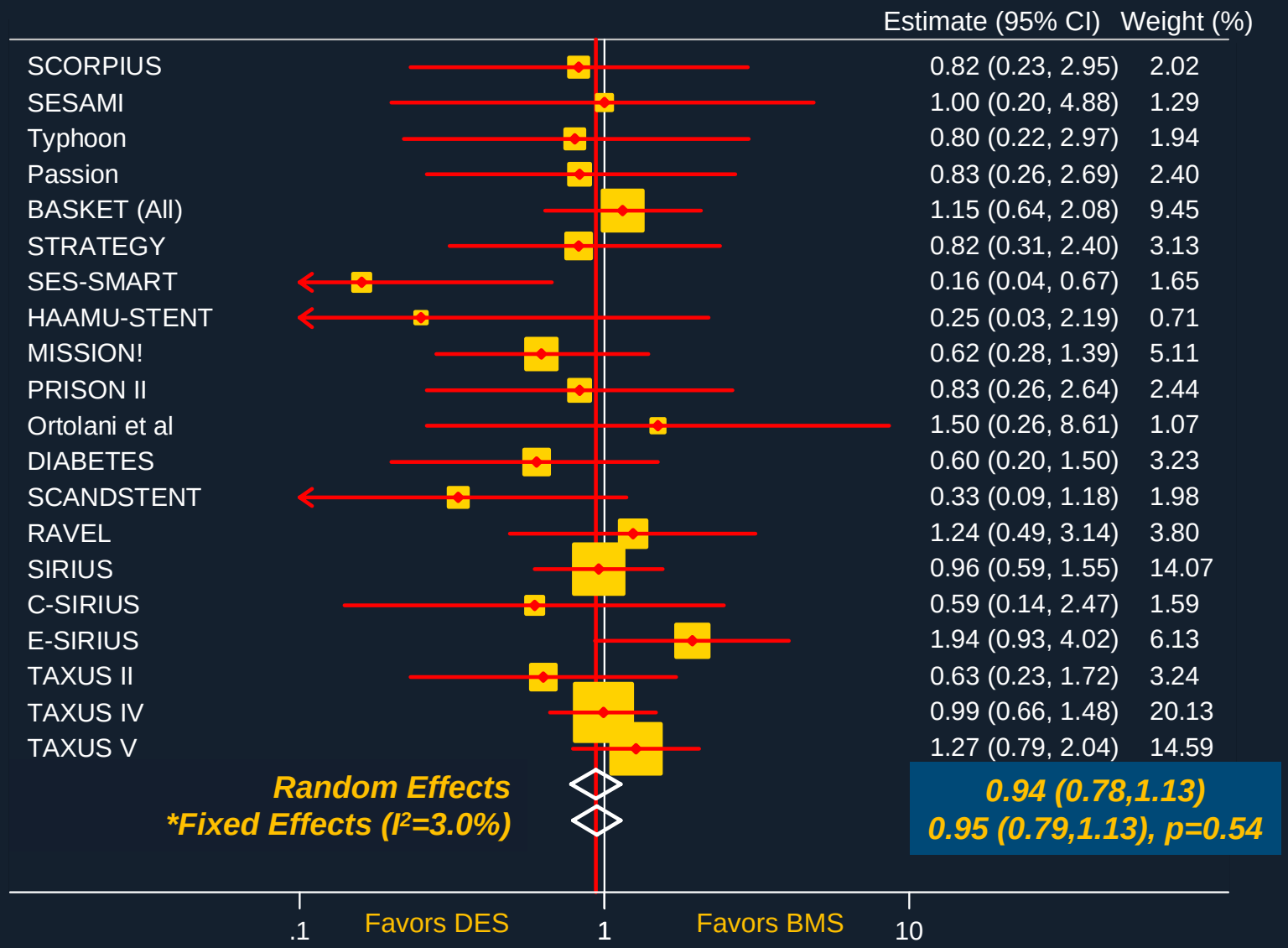
All-Cause Mortality: SES/PES RCTs

8,867 patients, 21 trials, mean F/U 2.9 years



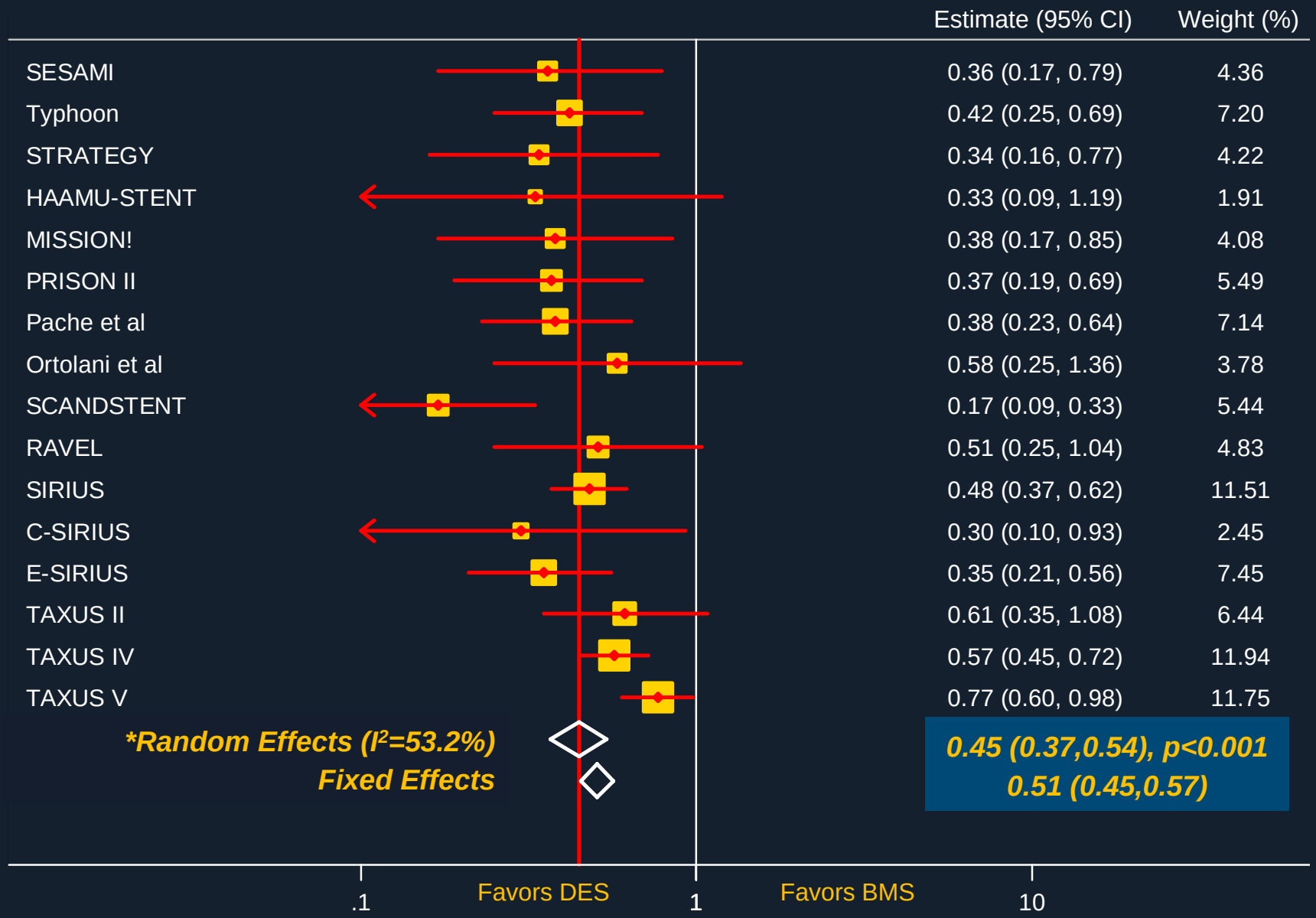
MI: SES/PES RCTs

8,850 patients, 20 trials , mean F/U 2.9 years



TVR: SES/PES RCTs

7,291 patients, 16 trials , mean F/U 3.2 years



HORIZONS AMI

Harmonizing Outcomes with Revascularization and Stents in AMI

3602 pts with STEMI with symptom onset ≤12 hours

Aspirin, thienopyridine

R 1:1

- **UFH + GP IIb/IIIa inhibitor (abciximab or eptifibatide)**
- **Bivalirudin monotherapy (± provisional GP IIb/IIIa)**

Emergent angiography, followed by triage to…

CABG – Primary PCI – Medical Rx

3000 pts eligible for stent randomization

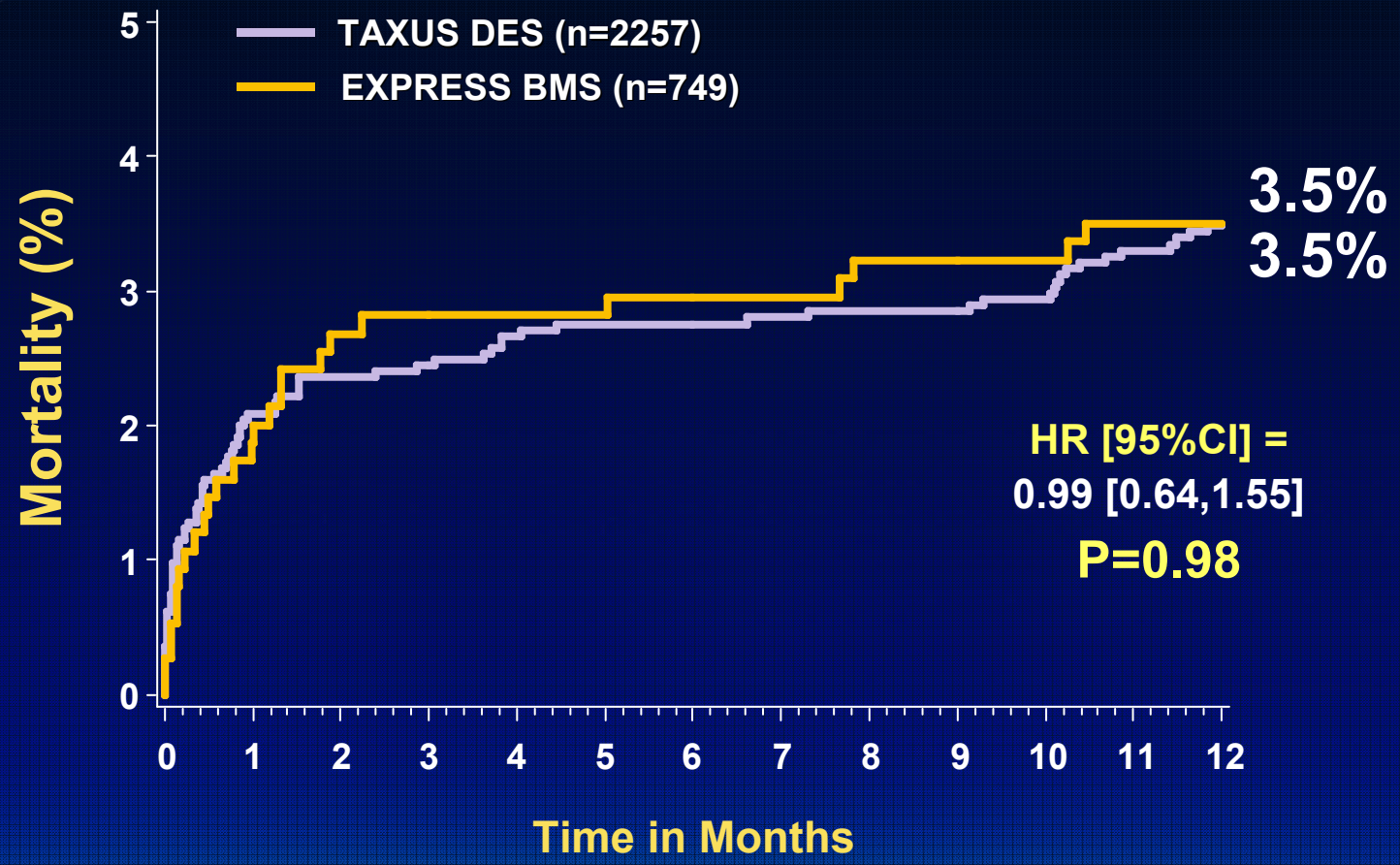
R 3:1

- **Paclitaxel-eluting TAXUS stent**
- **Bare metal EXPRESS stent**

Clinical FU at 30 days, 6 months, 1 year, and then yearly through 5 years; angio FU at 13 months

HORIZONS AMI

One-Year All-Cause Mortality

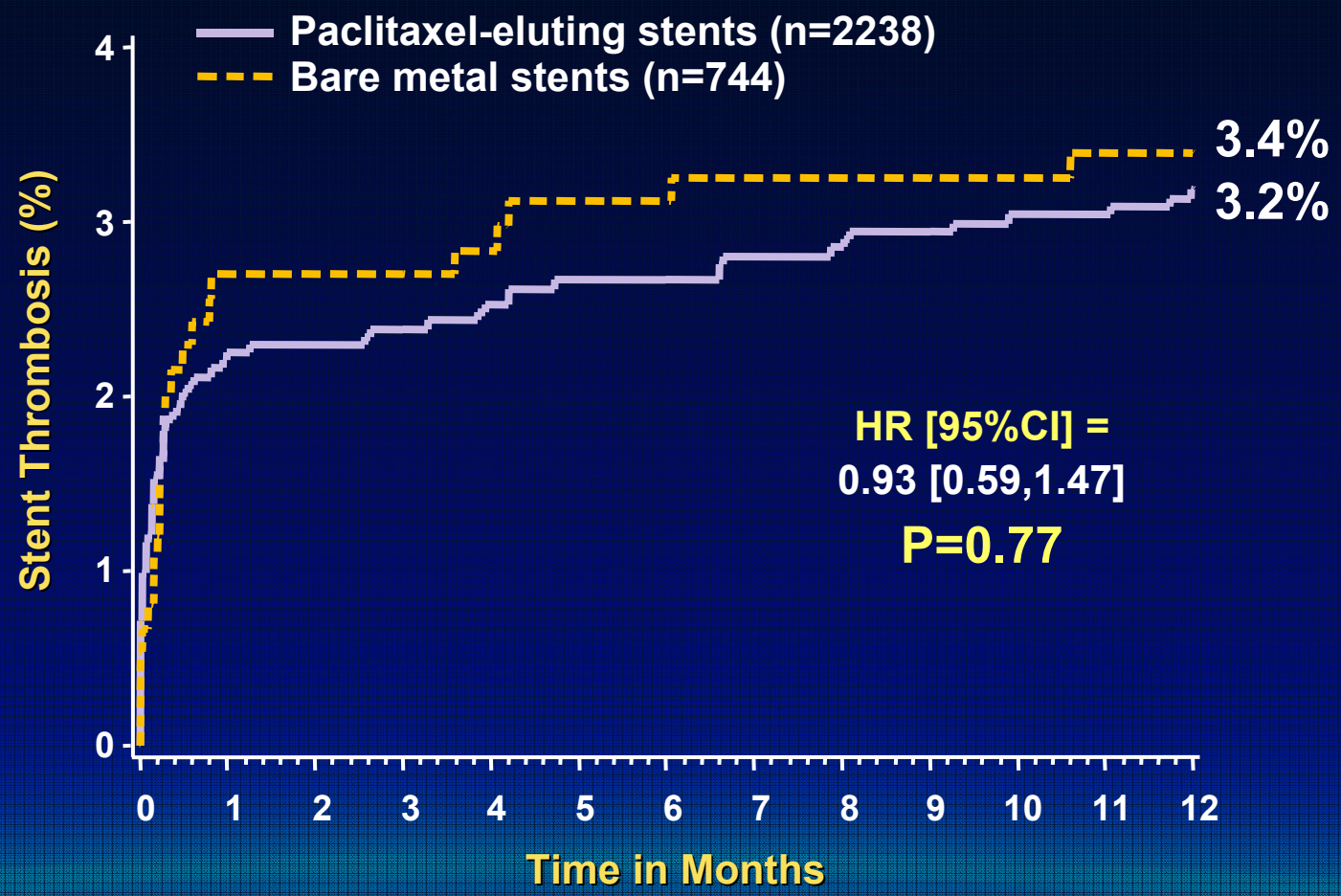


Number at risk					
TAXUS DES	2257	2180	2161	2147	1949
EXPRESS BMS	749	716	712	702	648

Stone GW et al. In press.

HORIZONS AMI

Stent Thrombosis
(ARC Definite or Probable)

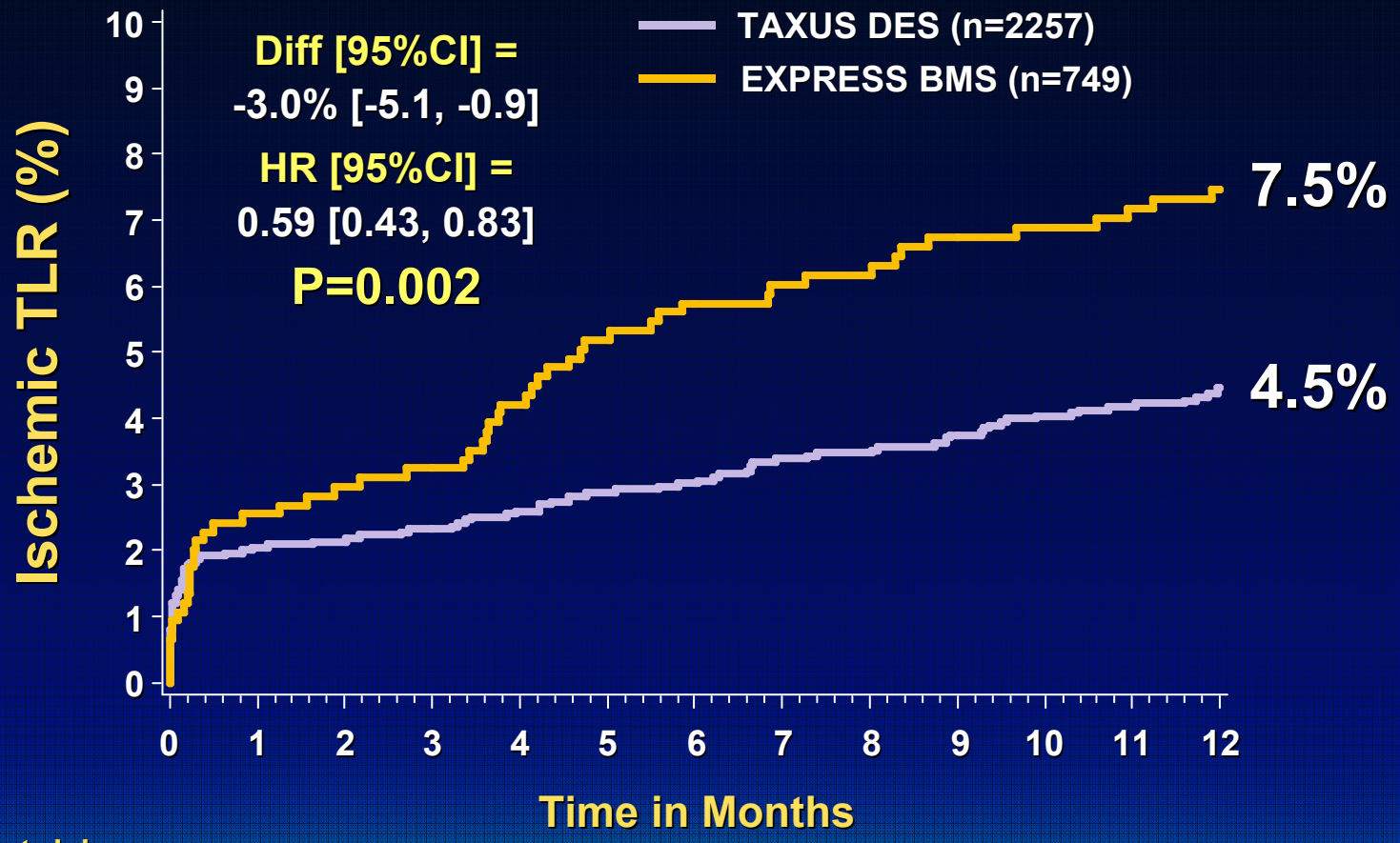


Number at risk					
PES	2238	2123	2098	2079	1885
BMS	744	701	694	683	629

Stone GW et al. In press.

HORIZONS AMI

Primary Efficacy Endpoint: Ischemic TLR



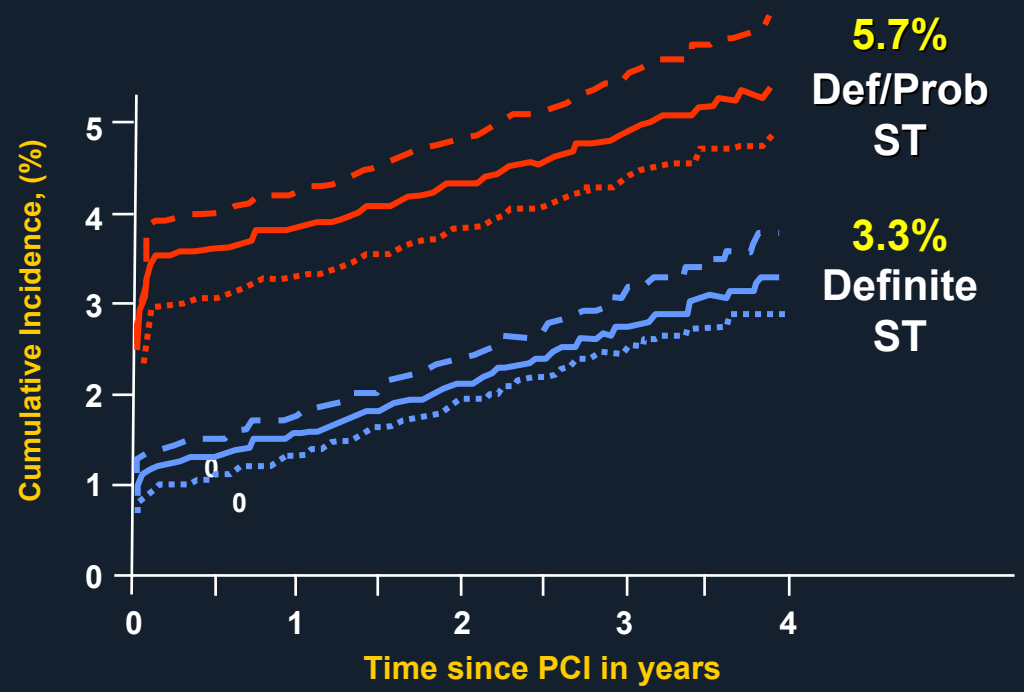
Number at risk					
TAXUS DES	2257	2132	2098	2069	1868
EXPRESS BMS	749	697	675	658	603

Stone GW et al. In press.

HORIZONS AMI

DES Thrombosis in the "Real World"

- 8,146 DES pts at 2 centers
- ST rate steady 0.53% [95%CI 0.44%, 0.64%] per yr between 30 d and 4 yrs

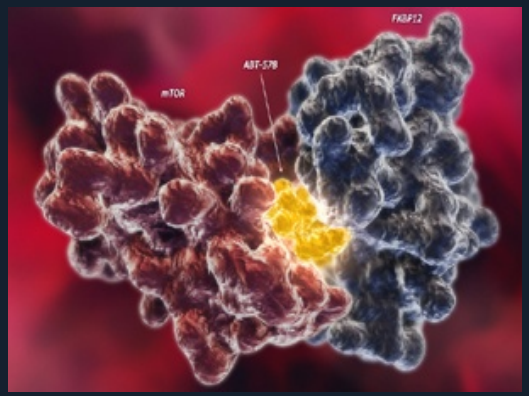


Months	1	12	24	36	48
Cumulative incidence definite ST, %	1.2	1.6	2.1	2.7	3.3
Cumulative incidence probable and definite ST, %	3.7	4.1	4.6	5.2	5.7
Patients at risk	7537	7209	5157	2747	1051

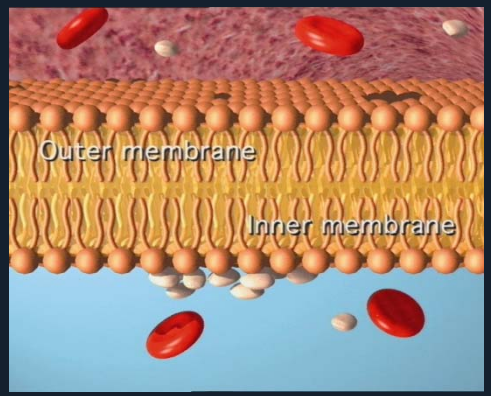
Wenaweser P et al. *JACC* 2008;52:1134–40

Drug-eluting Stents "Second Gen US"

Endeavor



Zotarolimus

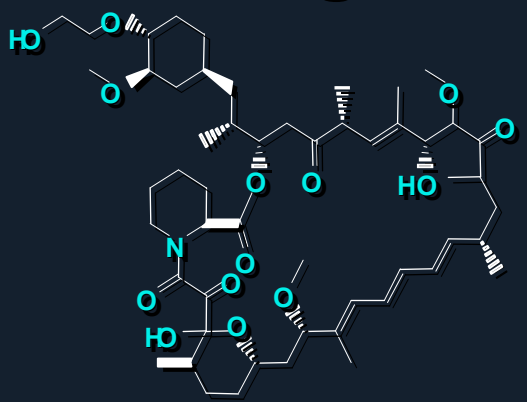


Phosphorylcholine

Driver

Drug | **Polymer** | **Stent**

Xience V*



Everolimus

VDF + HFP copolymer

Vision

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*AKA Promus

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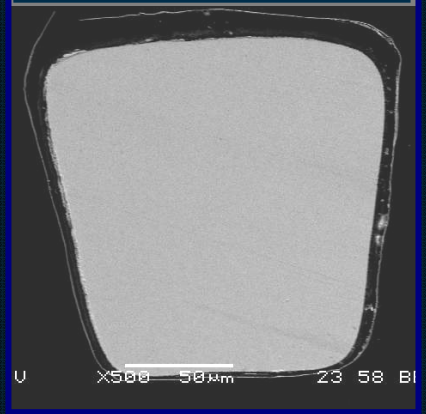
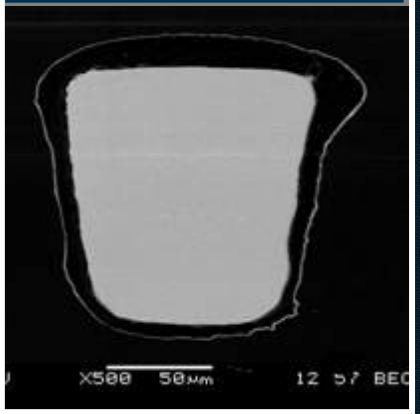
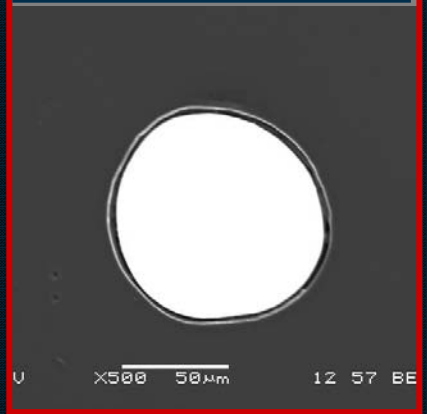
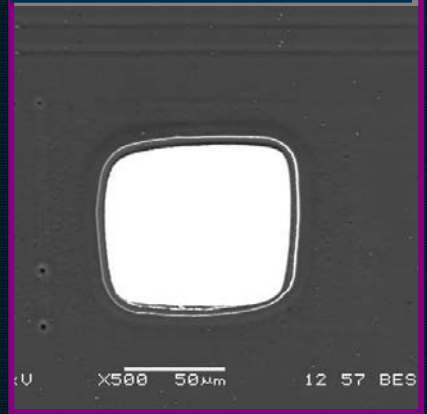
DES Strut and Polymer Thickness

3.0 mm diameter stents, 500x magnification

CYPHER®	TAXUS®	ENDEAVOR™	XIENCE™ V
			
Strut Thickness: **140 µm**	Strut Thickness: **132 µm**	Strut Thickness: **91 µm**	Strut Thickness: **81 µm**
Polymer Thickness: **12.6 µm**	Polymer Thickness: **16 µm**	Polymer Thickness: **5.3 µm**	Polymer Thickness: **7.8 µm**
Total: 152.6 um	**Total: 148 um**	**Total: 96.3 um**	**Total: 88.8 um**

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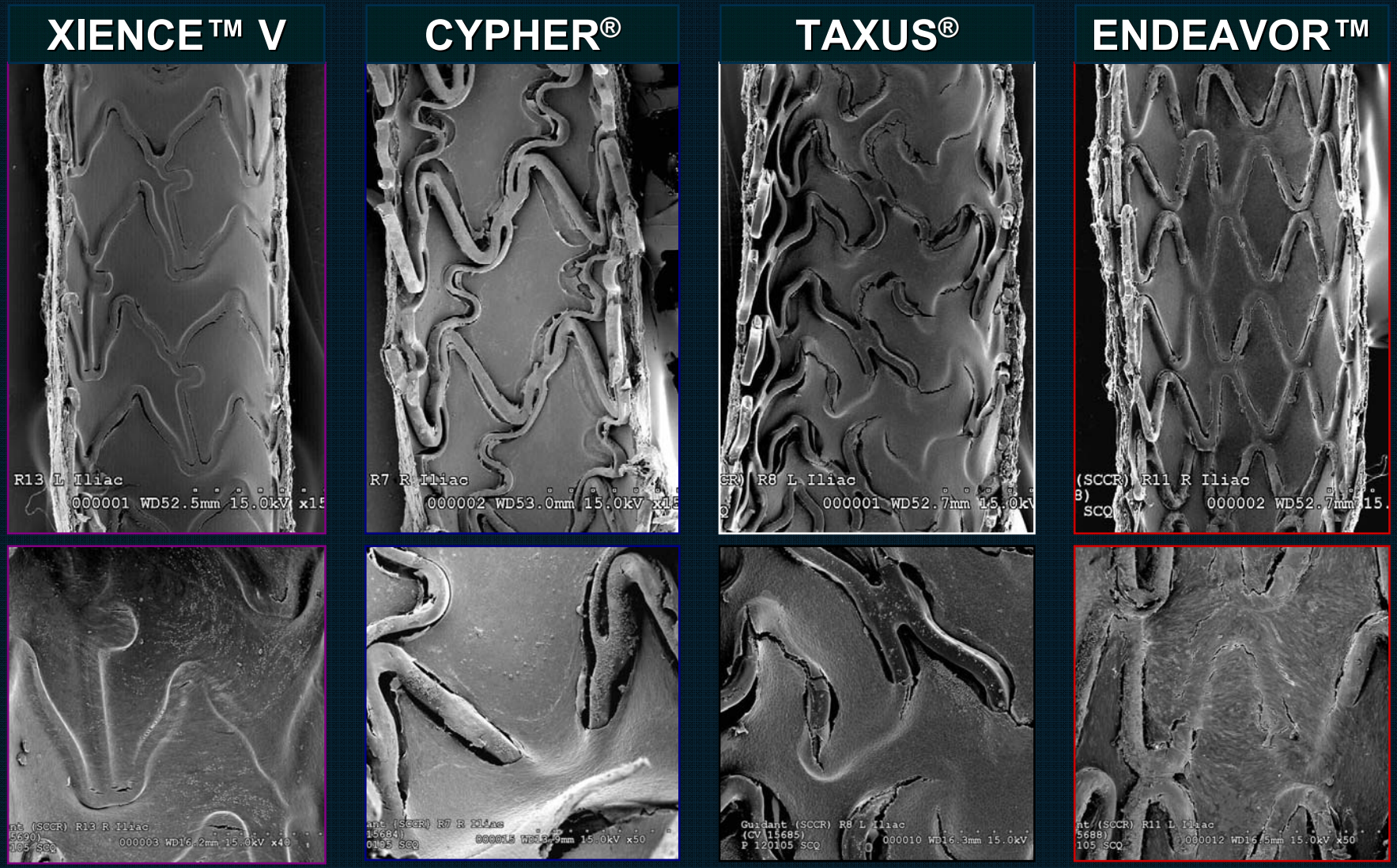
14 Day Endothelialization: Rabbit Iliac Model



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Joner M et al. JACC 2008;52:333-42

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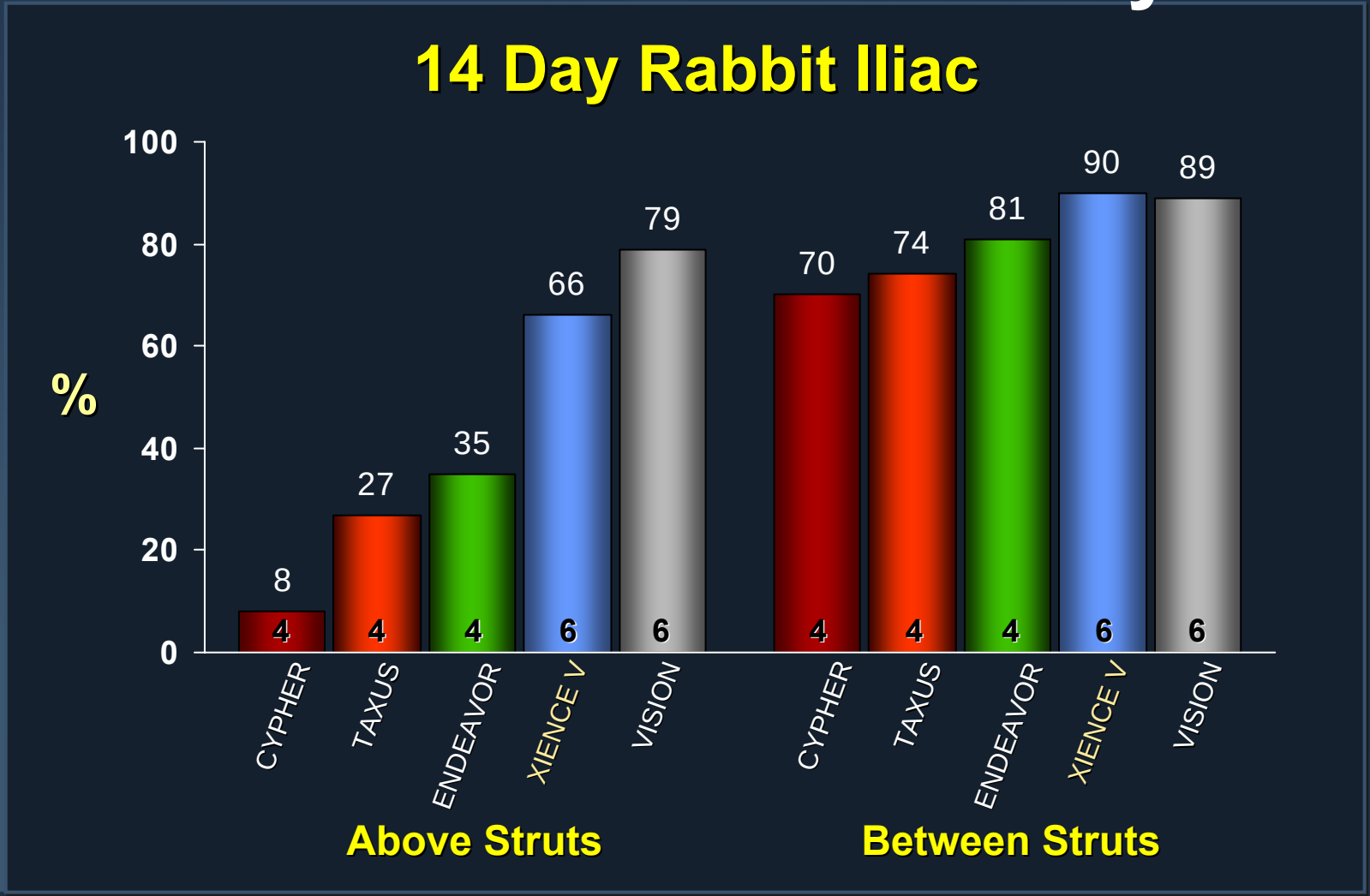
Quantitative Assessment of Luminal Endothelialization by SEM



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Joner M et al. JACC 2008;52:333-42

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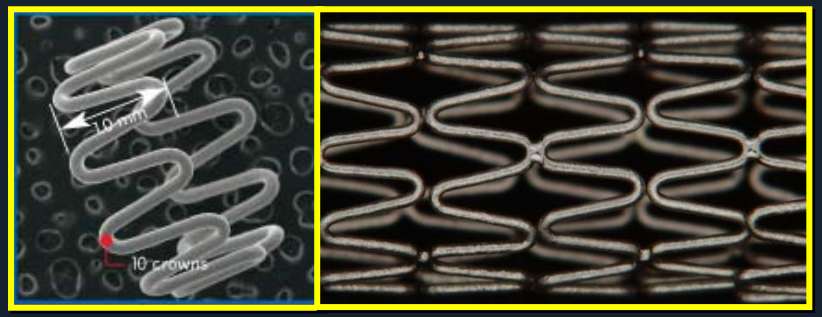
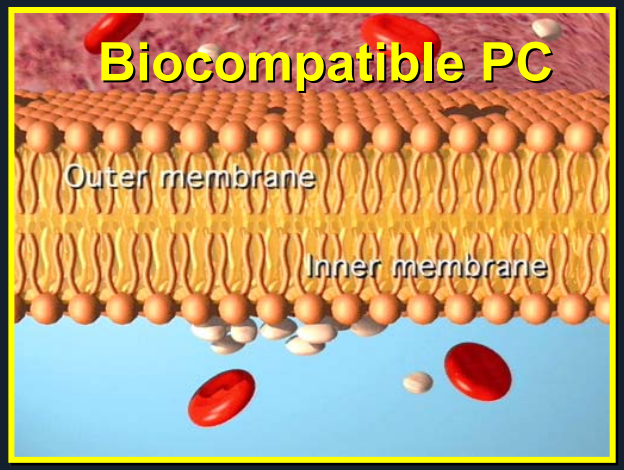
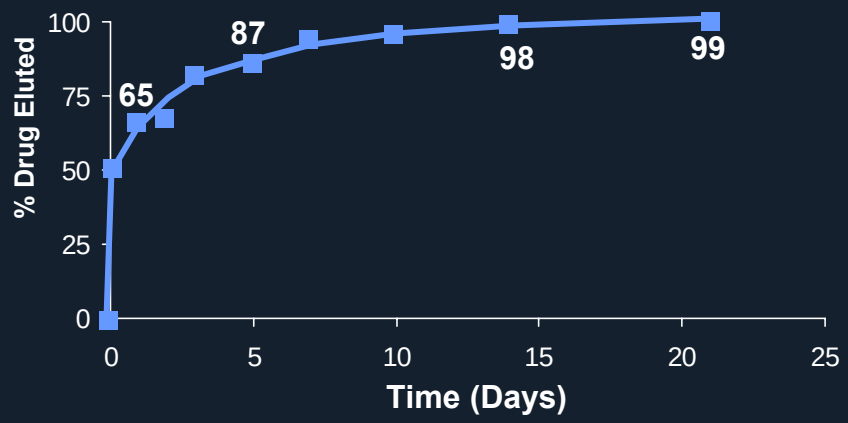
ENDEAVOR Safety Considerations
Design Features

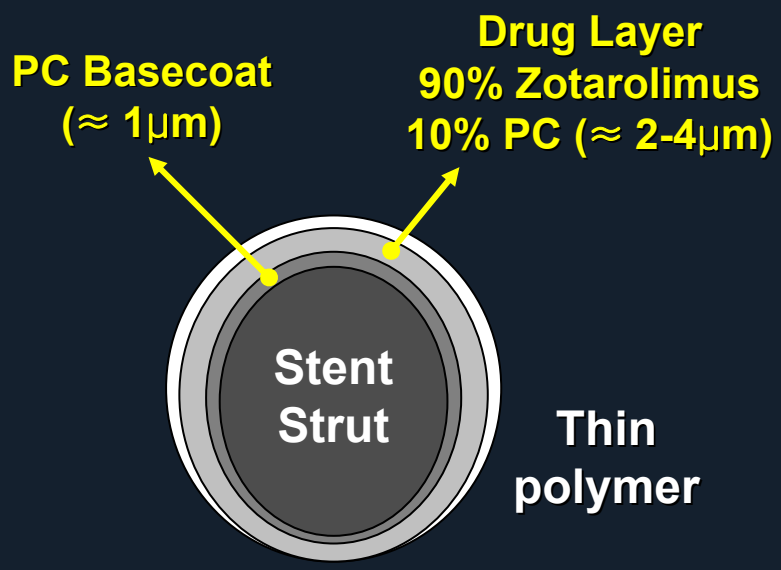


Stent design = reduced injury
(rounded thin struts)





Rapid drug elution



ENDEAVOR IV (N=1,548)

Clinical Trial Design
PI: Martin B. Leon

Single De Novo Native Coronary Lesion
Vessel Diameter: 2.5–3.5 mm
Lesion Length: ⩽ 27 mm
Pre-dilatation required

Endeavor Stent
n = 774

1:1 randomization
N = 1,548 patients
80 sites
US

Taxus Stent
n = 774

Clinical/MACE

30d | 6mo | 8mo | 9mo | 12mo | 2yr | 3yr | 4yr | 5yr

Angiography/IVUS

QCA and IVUS
Subset
(328 total = 21.2%)

Primary Endpoint: TVF at 9 months
Secondary Endpoints: In-segment % DS at 8 months; TLR and TVR at 9 months
Drug Therapy: ASA and Clopidogrel/Ticlid >6 months
Zotarolimus Dose: 10 μg per mm stent length

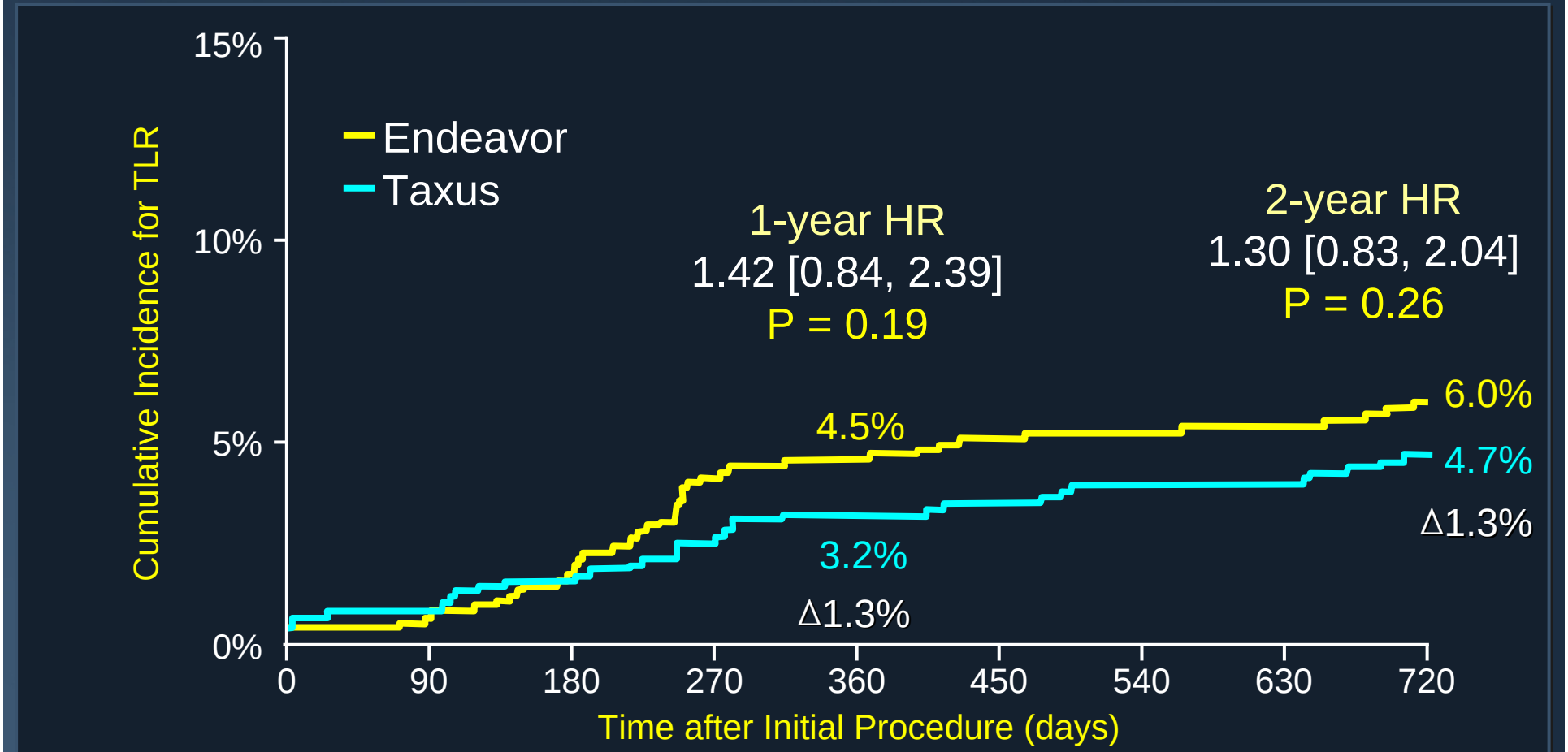
Leon MB. TCT 2008.

Endeavor IV
8 Month QCA (n=279)

	Endeavor (144 pts)	Taxus (135 pts)	*P value*
FU RVD (mm)	2.65 ± 0.47	2.68 ± 0.45	0.64
Late loss (mm)			
In-stent	0.67 ± 0.49	0.42 ± 0.50	<0.001
In-segment	0.36 ± 0.47	0.23 ± 0.45	0.02
FU MLD (mm)			
In-stent	1.95 ± 0.61	2.25 ± 0.61	<0.001
In-segment% DS	1.80 ± 0.55	1.98 ± 0.56	0.008
FU % DS			
In-stent	26.41 ± 19.74	16.09 ± 17.99	<0.001
In-segment	32.28 ± 17.02	26.61 ± 15.52	0.004
Binary restenosis			
In-stent	13.3% (19)	6.7% (9)	0.08
In-segment	15.3% (22)	10.4% (14)	0.28

Leon MB. TCT 2008.

ENDEAVOR IV – 2yr FU
TLR to 24 months



Endeavor	**773**	**773**	**755**	**744**	**706**	**684**	**666**	**661**	**654**
Taxus	**775**	**771**	**757**	**740**	**708**	**687**	**668**	**663**	**660**

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Leon MB. TCT 2008.

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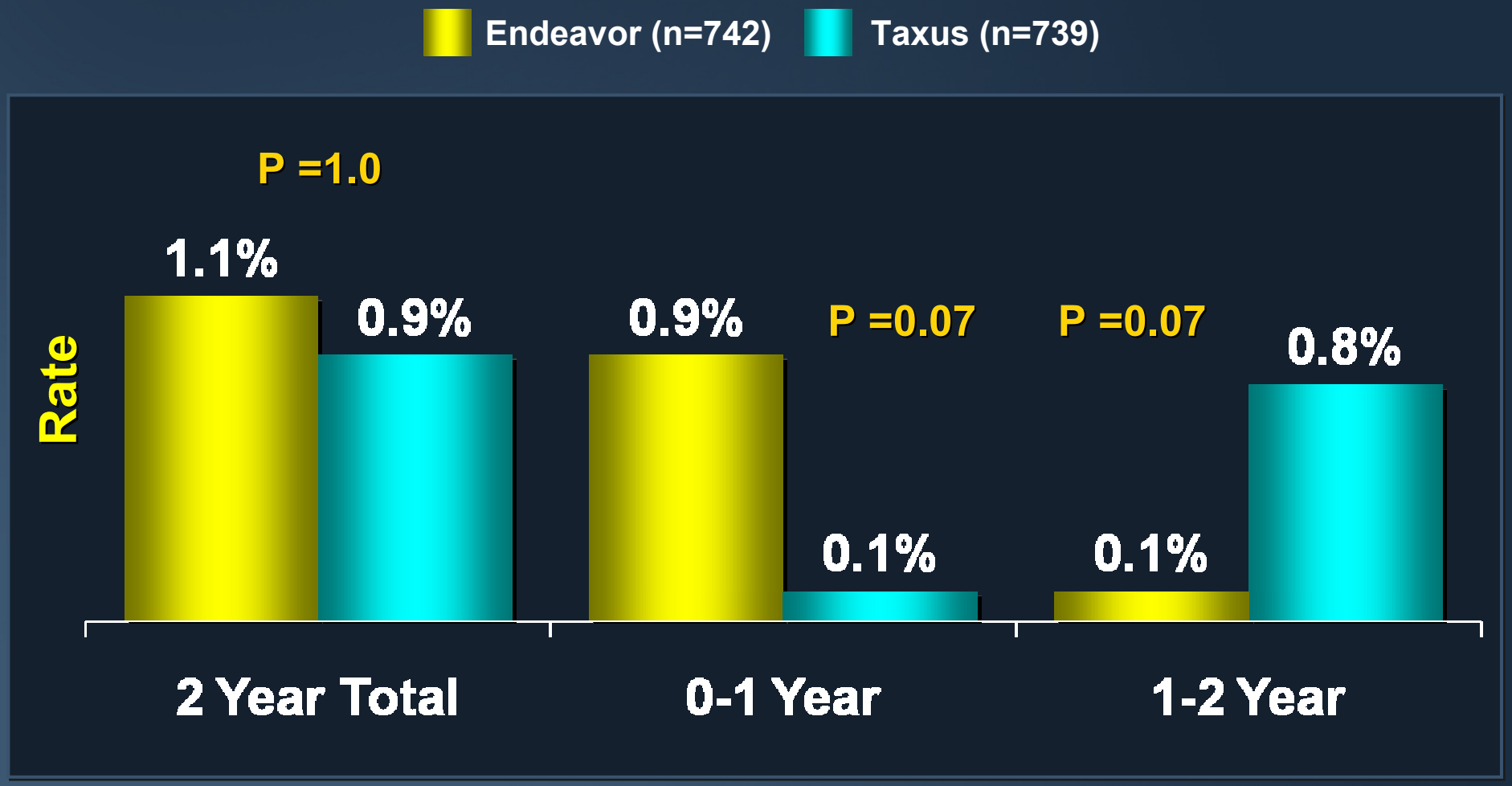
ENDEAVOR IV – 2yr FU
Clinical Events at 24 months

	Endeavor n = 742	Taxus n = 739	*P* value
Death (all)	3.1% (23)	2.6% (19)	0.64
Cardiac	1.5% (11)	1.2% (9)	0.82
MI (all)	2.0% (15)	4.1% (30)	0.02
Q Wave	0.4% (3)	0.5% (4)	0.73
Non Q Wave	1.6% (12)	3.5% (26)	0.02
Death (cardiac) + MI (all)	3.4% (25)	5.1% (38)	0.10
TLR	5.9% (44)	4.6% (34)	0.30
TVR (non-TL)	4.2% (31)	5.8% (43)	0.15
TVR	8.9% (66)	9.2% (68)	0.86
MACE	9.8% (73)	10.0% (74)	0.93
TVF	11.1% (82)	13.1% (97)	0.23

Leon MB. TCT 2008.

ENDEAVOR IV – 2yr FU
Stent Thrombosis (ARC Def/Prob)



Leon MB. TCT 2008.

SORT-OUT III

2,333 unselected pts randomized at 5 Danish centers between 1/06 and 8/07

PCI Indication

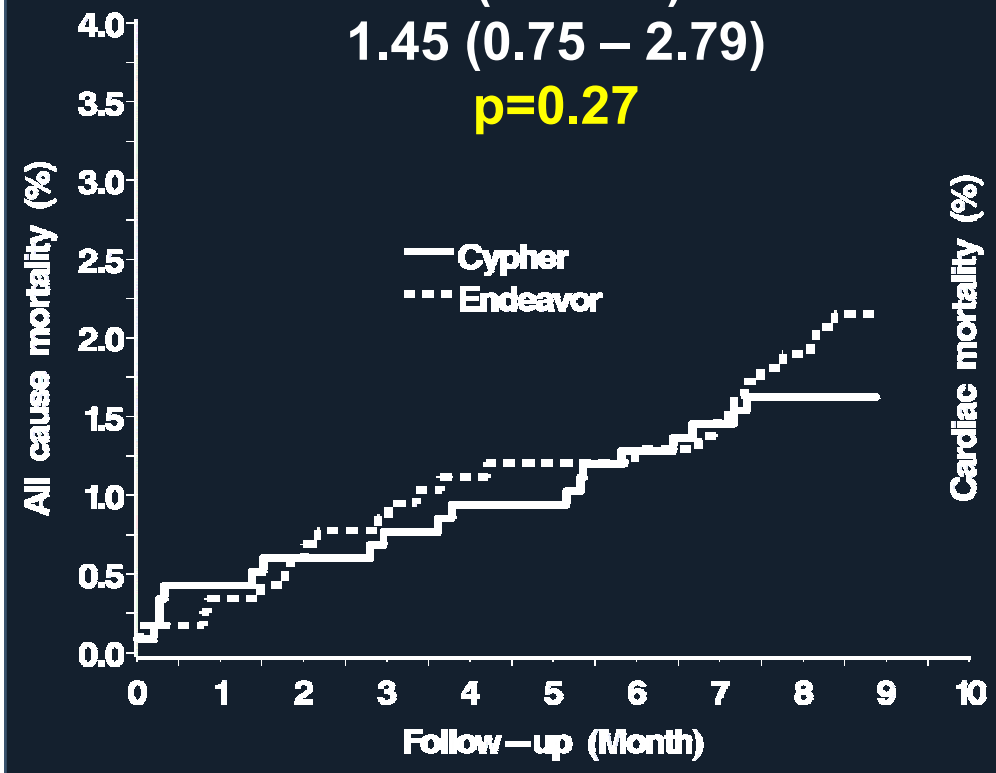
	Cypher N=1171	Endeavor N=1162	P
Stable angina	50.6%	52.8%	ns
NSTEMI/UAP	38.1%	37.5%	ns
STEMI	8.5%	6.0%	ns
Other	2.7%	3.6%	ns

Lassen JF. TCT 2008.

SORT-OUT III

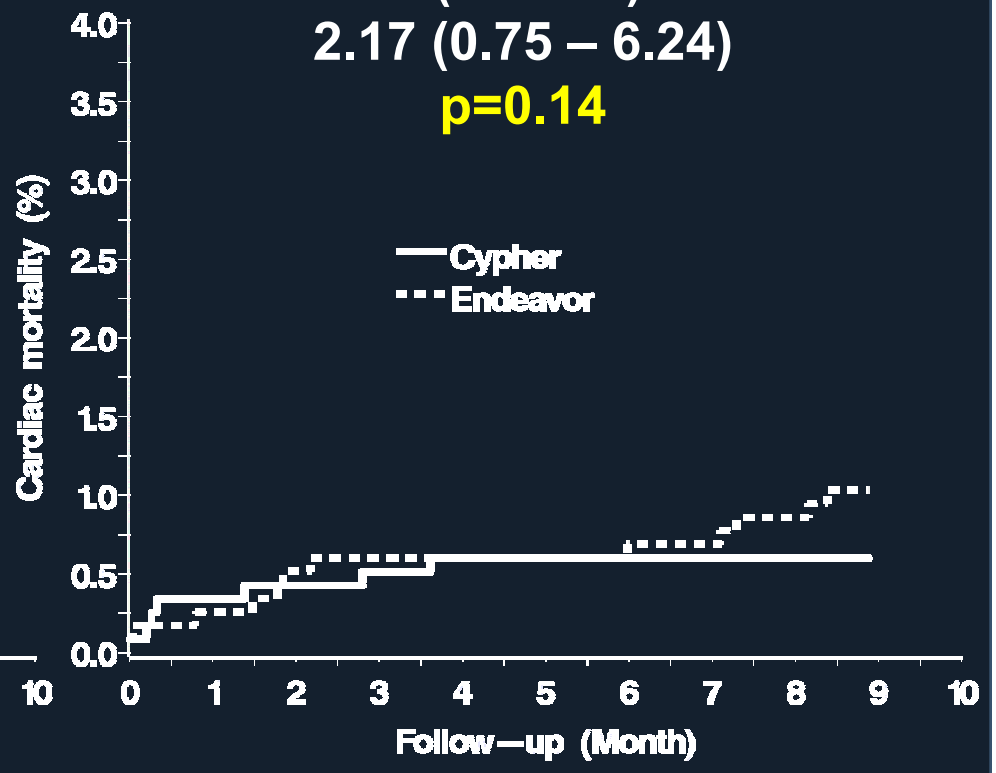
All Cause Mortality

HR (95% CI) =
1.45 (0.75 – 2.79)
p=0.27



Cardiac Mortality

HR (95% CI) =
2.17 (0.75 – 6.24)
p=0.14

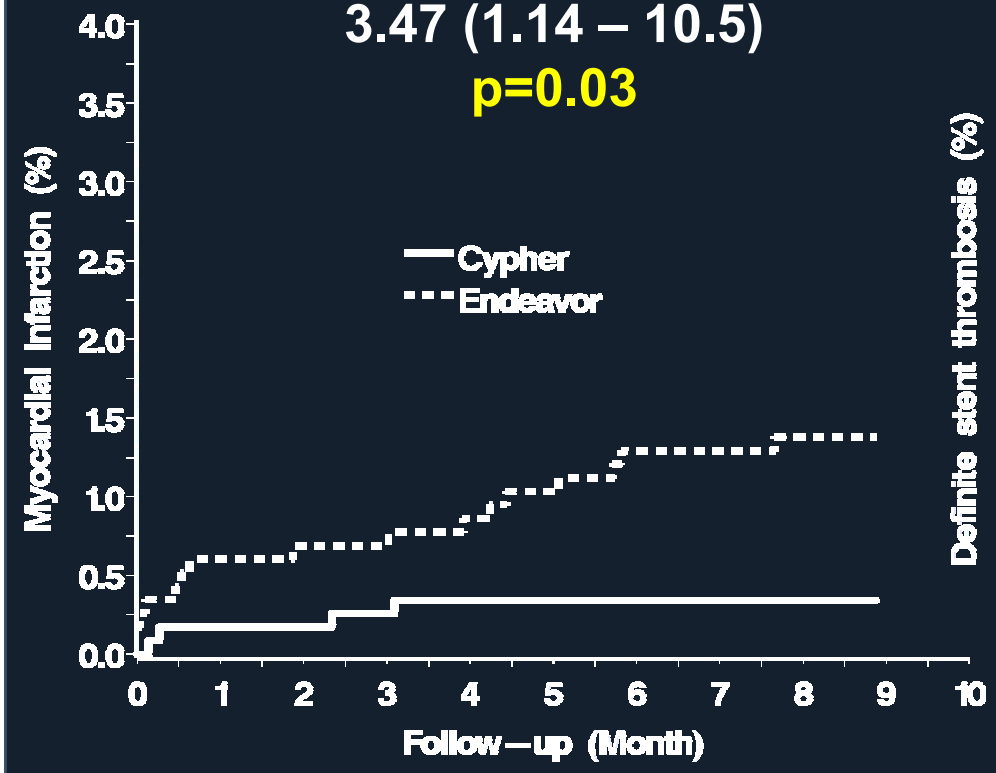


Lassen JF. TCT 2008.

SORT-OUT III

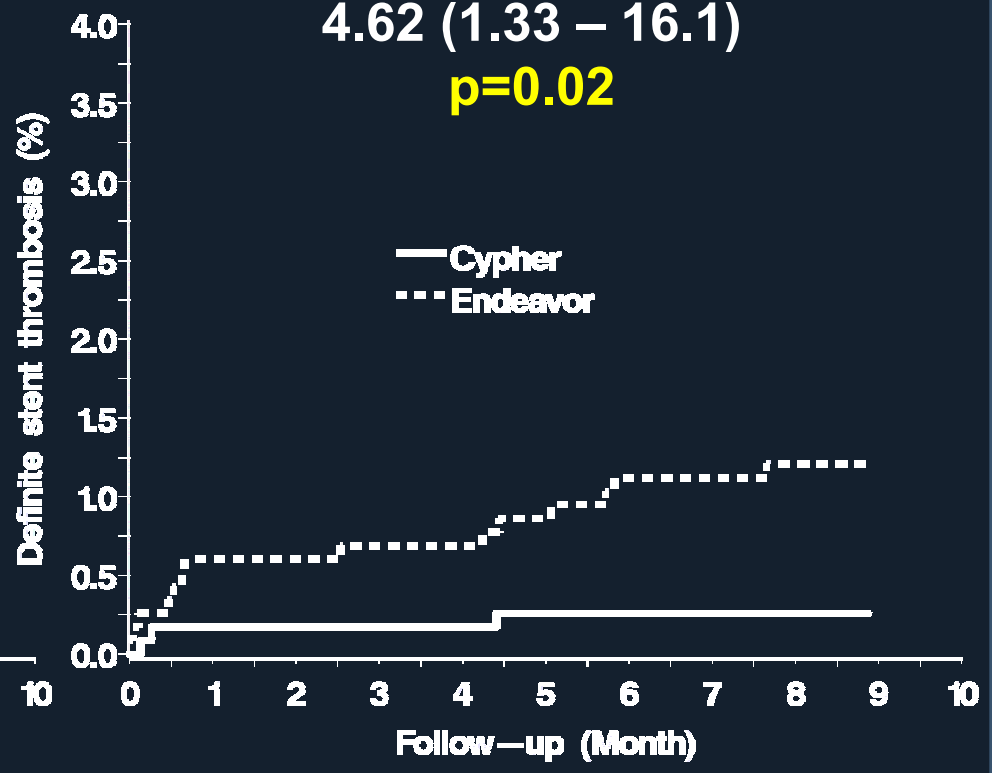
Myocardial Infarction

HR (95% CI) =
3.47 (1.14 – 10.5)
p=0.03



Definite Stent Thrombosis

HR (95% CI) =
4.62 (1.33 – 16.1)
p=0.02

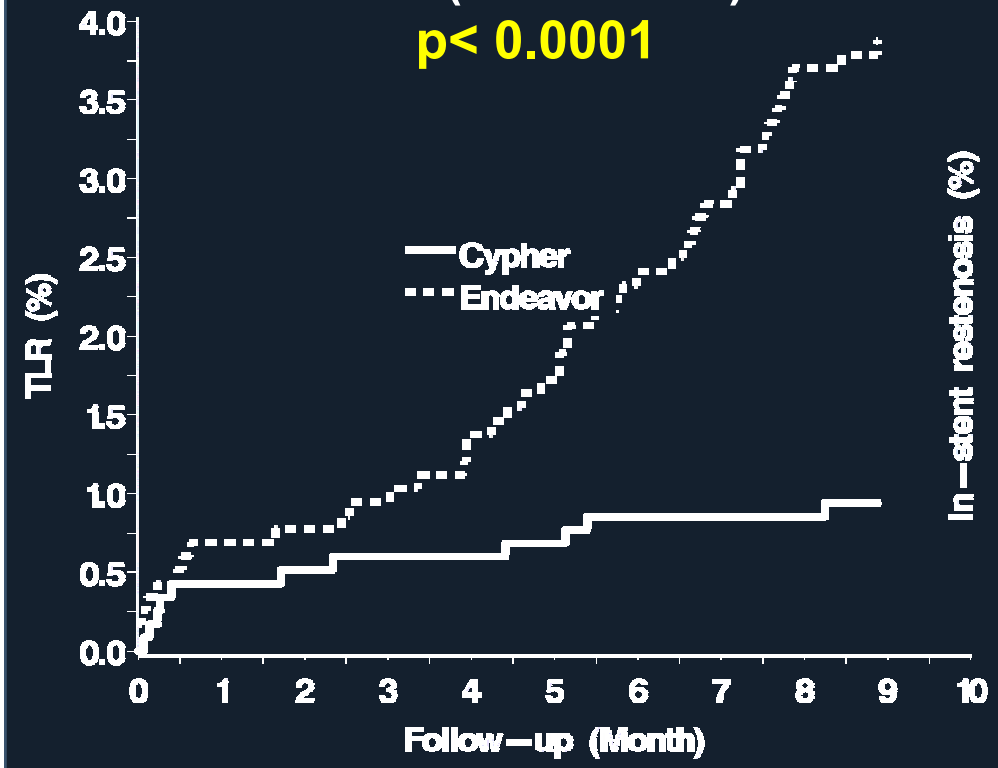


Lassen JF. TCT 2008.

SORT-OUT III

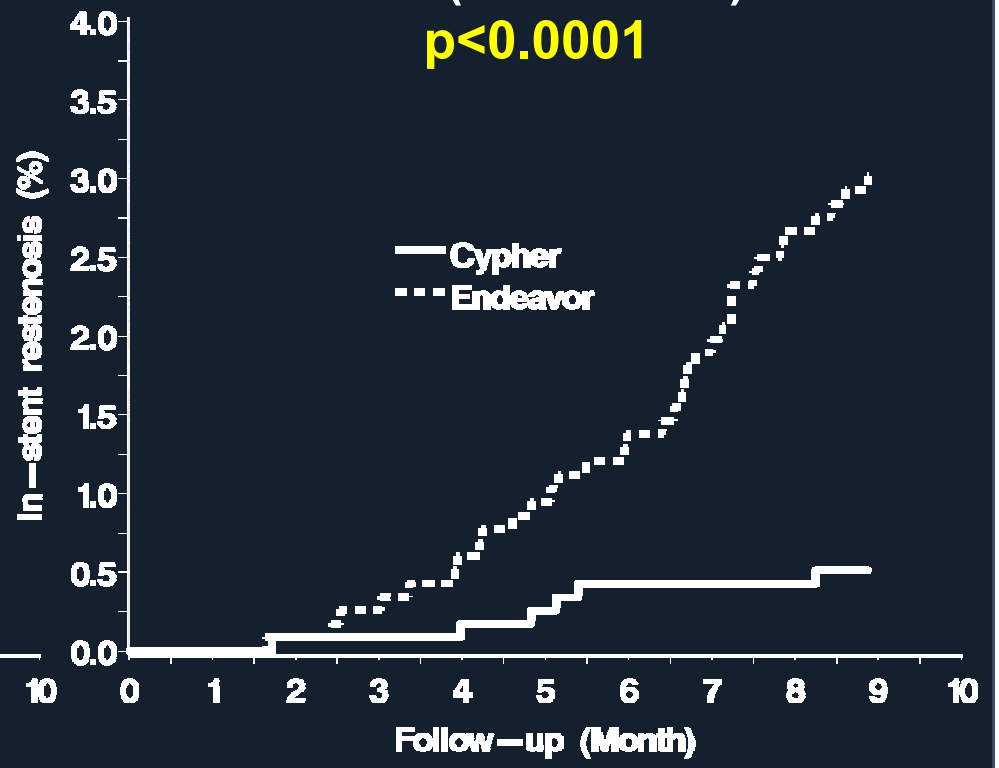
Target Lesion Revascularization

HR (95% CI) =
4.19 (2.10 – 8.35)
p< 0.0001



Clinically Significant Restenosis

HR (95% CI) =
6.59 (2.57 – 16.9)
p<0.0001



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Lassen JF. TCT 2008.

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ZEST Study Design

All Comer requiring PCI with DES for coronary lesions
in 19 Centers of Korea
(Total 2,640 patients)

Randomize 1:1:1
stratified by 1) Sites, 2) Diabetes, 3) Long lesions (≥ 28 mm)

ENDEAVOR®
(N=880)

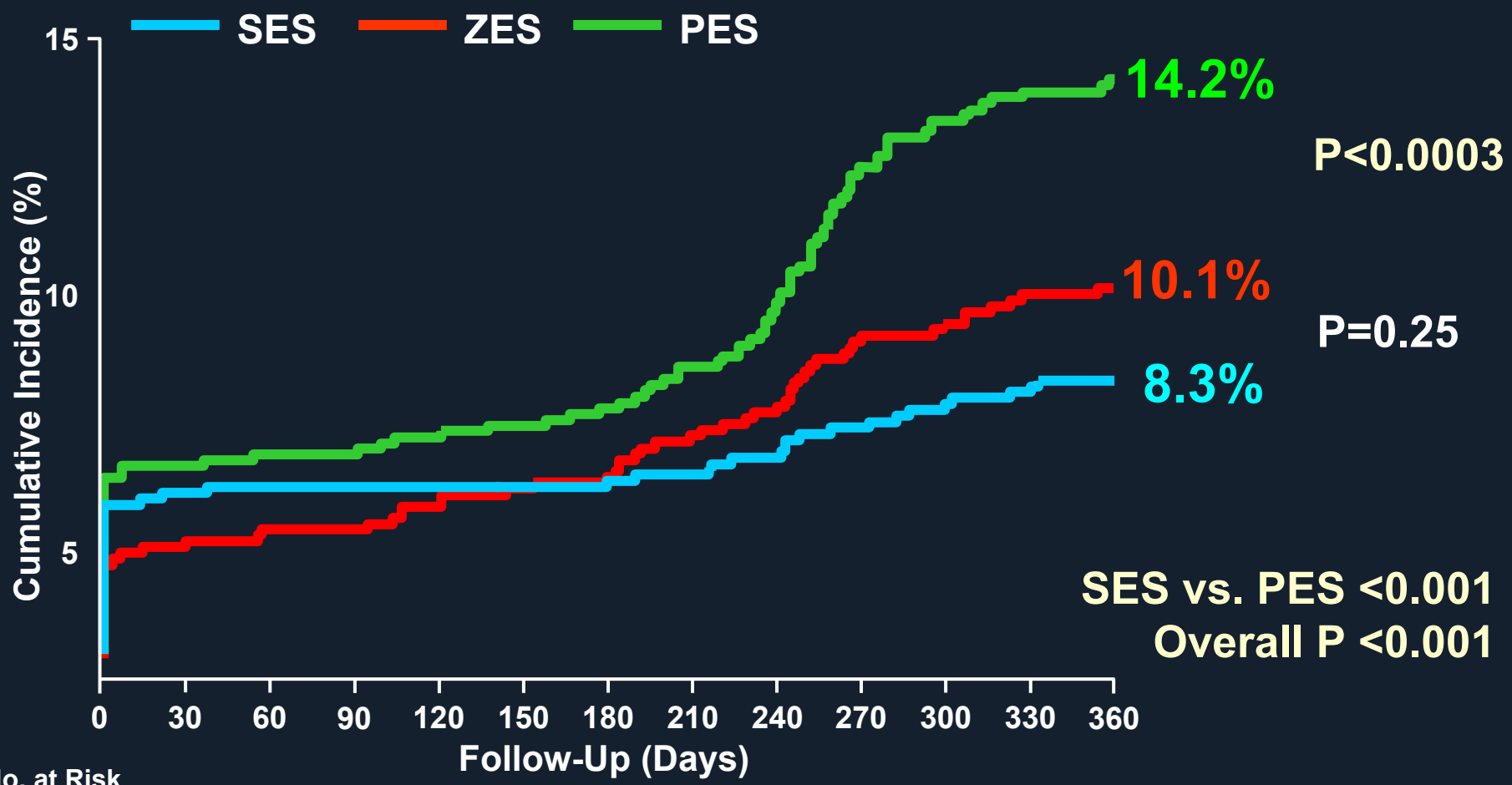
CYPER®
(N=880)

TAXUS Liberte™
(N=880)

Clinical follow-up at 12 months
Angiographic follow-up at 9 months

ZEST: Death, MI, Ischemia-driven TVR

Primary End Point at 12 month

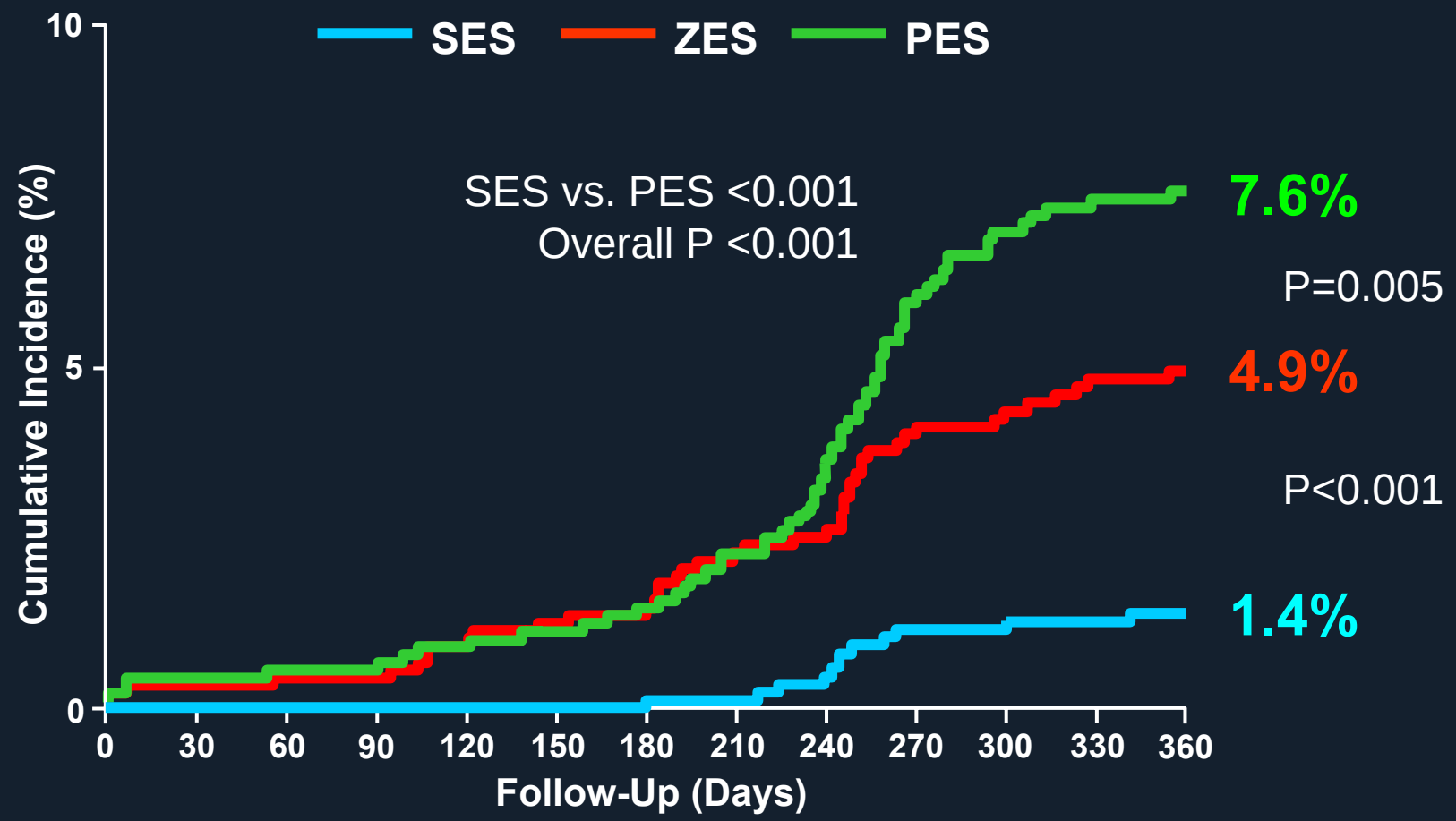


No. at Risk

ZES	883	827	816	790	782
SES	878	816	813	802	792
PES	884	821	808	763	745

Park SJ. ACC 2009

ZEST: Ischemic-driven TLR



No. at Risk

ZES	883	868	857	829	822
SES	878	869	866	853	845
PES	884	875	861	813	794

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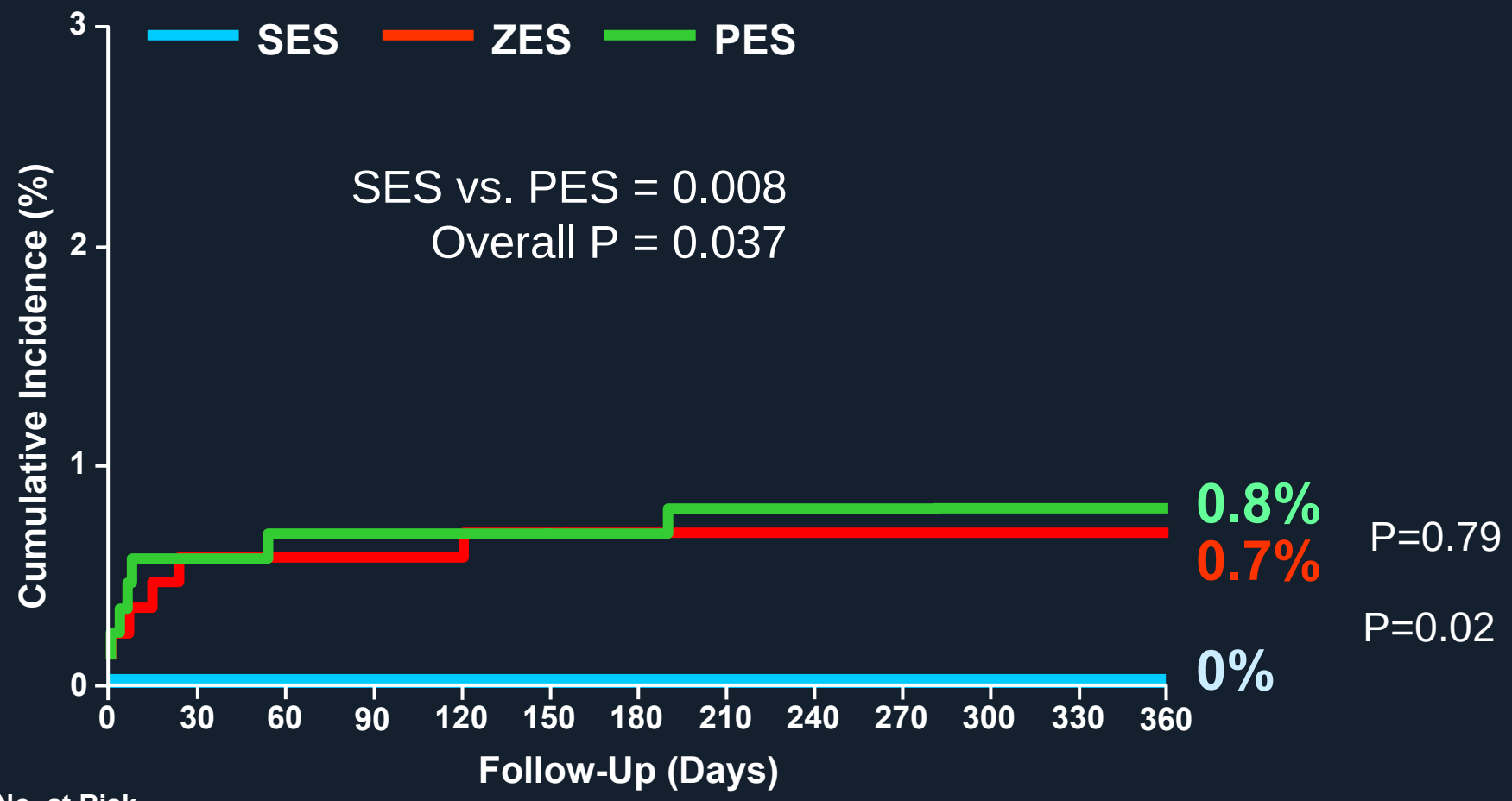
ZEST: Stent Thrombosis

ARC Definite or Probable Criteria



No. at Risk

ZES	883	869	866	861	861
SES	878	869	867	863	857
PES	884	875	868	859	853

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PROTECT

International RCT Designed to Estimate VLST (>1 year)

All Comer
Dual APT >3 to ≤12 months

Endeavor
N=4400

N = 8800
>200 International Sites
Randomization 1:1

Cypher
N=4400

Clinical FU

30d | 6mo | 12mo | 18mo | 24mo | 30mo | **3yr** | 4 yr | 5 yr

Primary Endpoint: ARC Definite or Probable Stent Thrombosis at 3 yrs

Principle Secondary Endpoints: Death/Non-Fatal MI, Cardiac death/Non-Fatal MI

Additional Endpoints: MACCE, TLR, TVR, Procedural Success

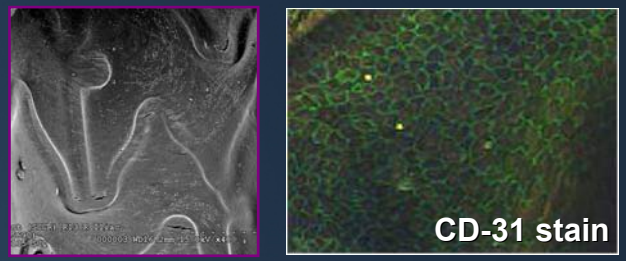
Clinical Follow up and Dual Antiplatelet Monitoring: At 30 days, and every 6 months until 3 years, than each year until 5 years

Enrollment Completed

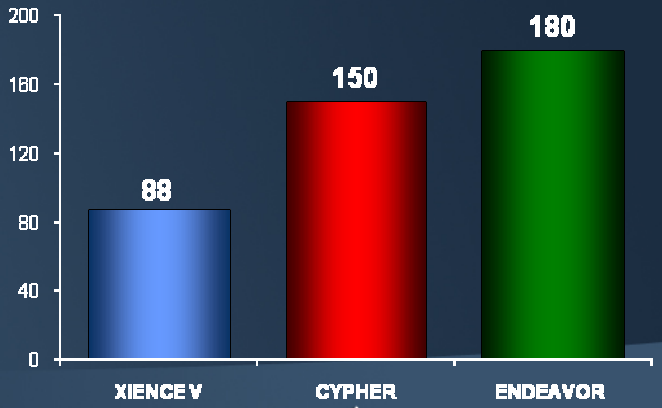
XIENCE V: Design Parameters and Pre-clinical Results

- Low profile, flexible, deliverable stent
- Highly resistant to strut fracture
- Thin, adhesive, inert durable polymer
  - promotes functional endothelialization
  - minimal bonding and webbing
  - no significant inflammation or hypersensitivity reaction
- Lowest dose of a "limus" on any DES

14 day endothelialization: Rabbit Iliac



Drug Load (mg) - 3.0 x 18 mm stents



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XIENCE V Randomized Trials
(Results reported)

SPIRIT FIRST RCT vs. VISION	SPIRIT II RCT vs. TAXUS	SPIRIT III RCT vs. TAXUS
Safety and performance	Clinical support for CE launch	Pivotal RCT with parallel registries
N = 60	N = 300	N = 1,002 rand
Europe	EU, India, NZ	USA
PI: PW Serruys	PI: PW Serruys	PI: GW Stone
4 year F/U completed	3 year F/U completed	2 year F/U completed

2 year pooled pt level analysis

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SPIRIT II + III Pooled Meta-analysis
Trial Descriptors
(1,302 randomized patients)

	SPIRIT II	SPIRIT III
# Rand. pts, sites	300 pts at 28 sites	1,002 pts at 65 sites
XIENCE V : Taxus	3:1 (223:77)	2:1 (669:333)
Geography	Europe, Asia	USA
RVD (mm)	2.5 – 4.0	2.5 – 3.75
Lesion length (mm)	≤ 28	≤ 28
# lesions, vessels	1-2 lesions, 1/vessel	1-2 lesions, 1/vessel
Clinical FU w/i 1st yr	1, 6, 9, 12 mos	1, 6, 9, 12 mos
Angio FU, completed	275/300 at 6 mos	436/564 at 8 mos

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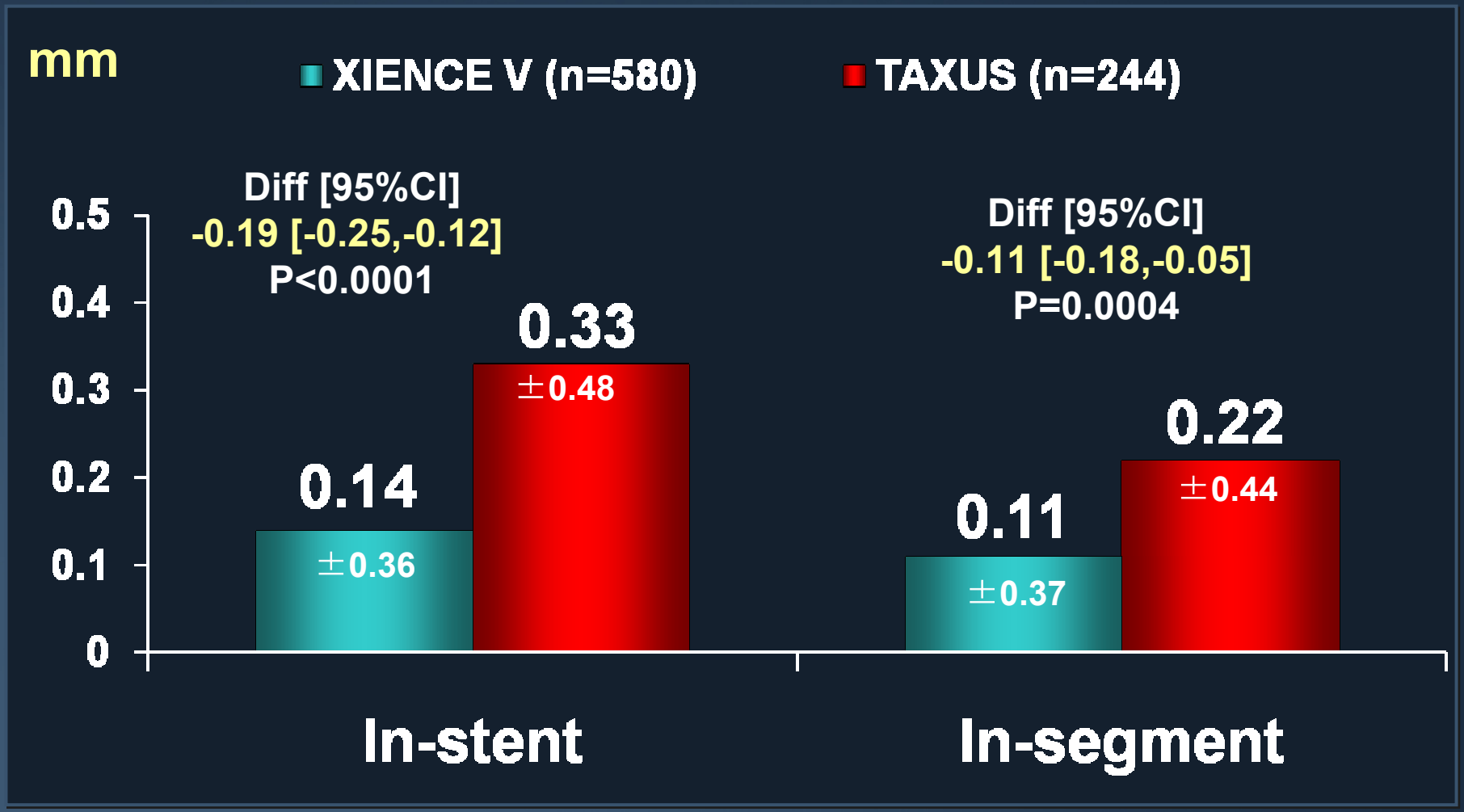
SPIRIT II + III Pooled Meta-analysis

Late Loss



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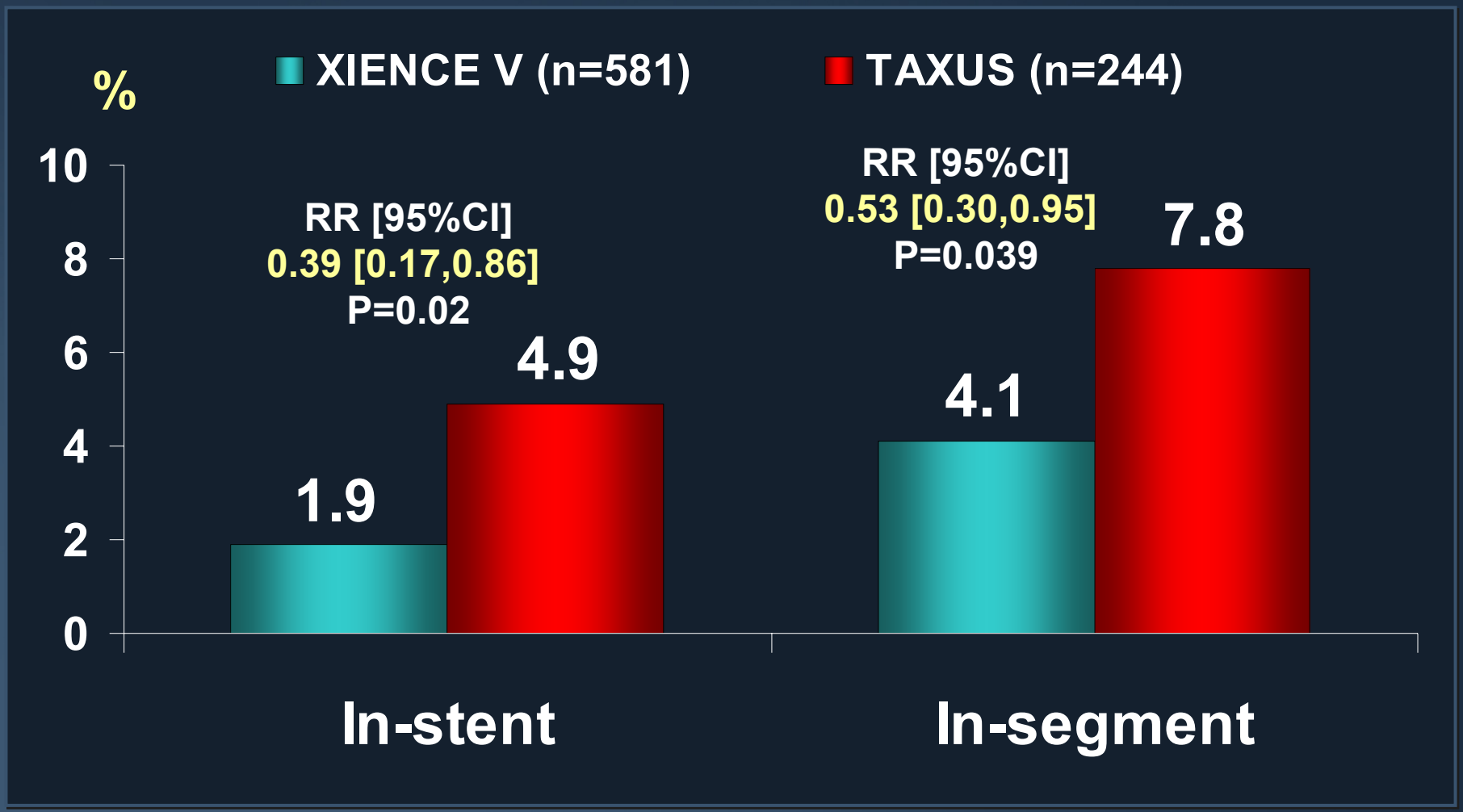
SPIRIT II + III Pooled Meta-analysis

Binary Restenosis



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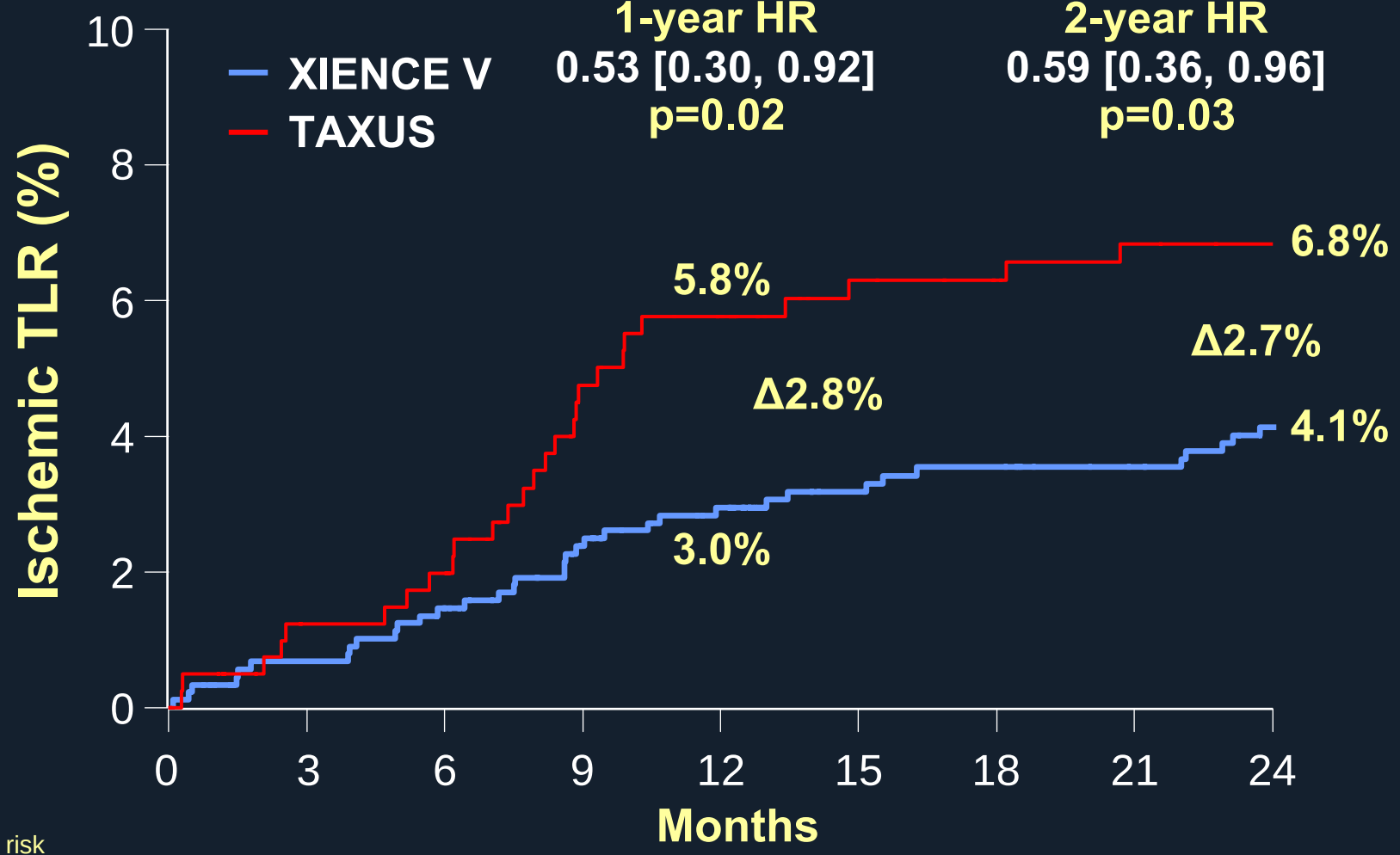
SPIRIT II + III: TLR



Number at risk									
XIENCE V	892	880	869	852	840	819	816	808	801
TAXUS	409	397	392	375	366	354	349	348	346

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SPIRIT II + III Pooled Meta-analysis

Stent Thrombosis

Definition	Xience V (N=892)	Taxus (N=410)	P value
Protocol*			
- Early (0-30 days)	0.3%	0%	
- Late (31 days – 1 year)	0.3%	0.8%	
- Very late (1 – 2 years)	0.5%	0.8%	
- TOTAL	1.2%	1.6%	0.59
ARC Definite/Probable			
- Early (0-30 days)	0.3%	0.2%	
- Late (31 days – 1 year)	0.3%	0.8%	
- Very late (1 – 2 years)	0.5%	0.8%	
- TOTAL	1.2%	1.6%	0.59

*ACS + angio thrombus, or unexplained death or STEMI/Q-wave MI in target lesion distribution w/i 30d

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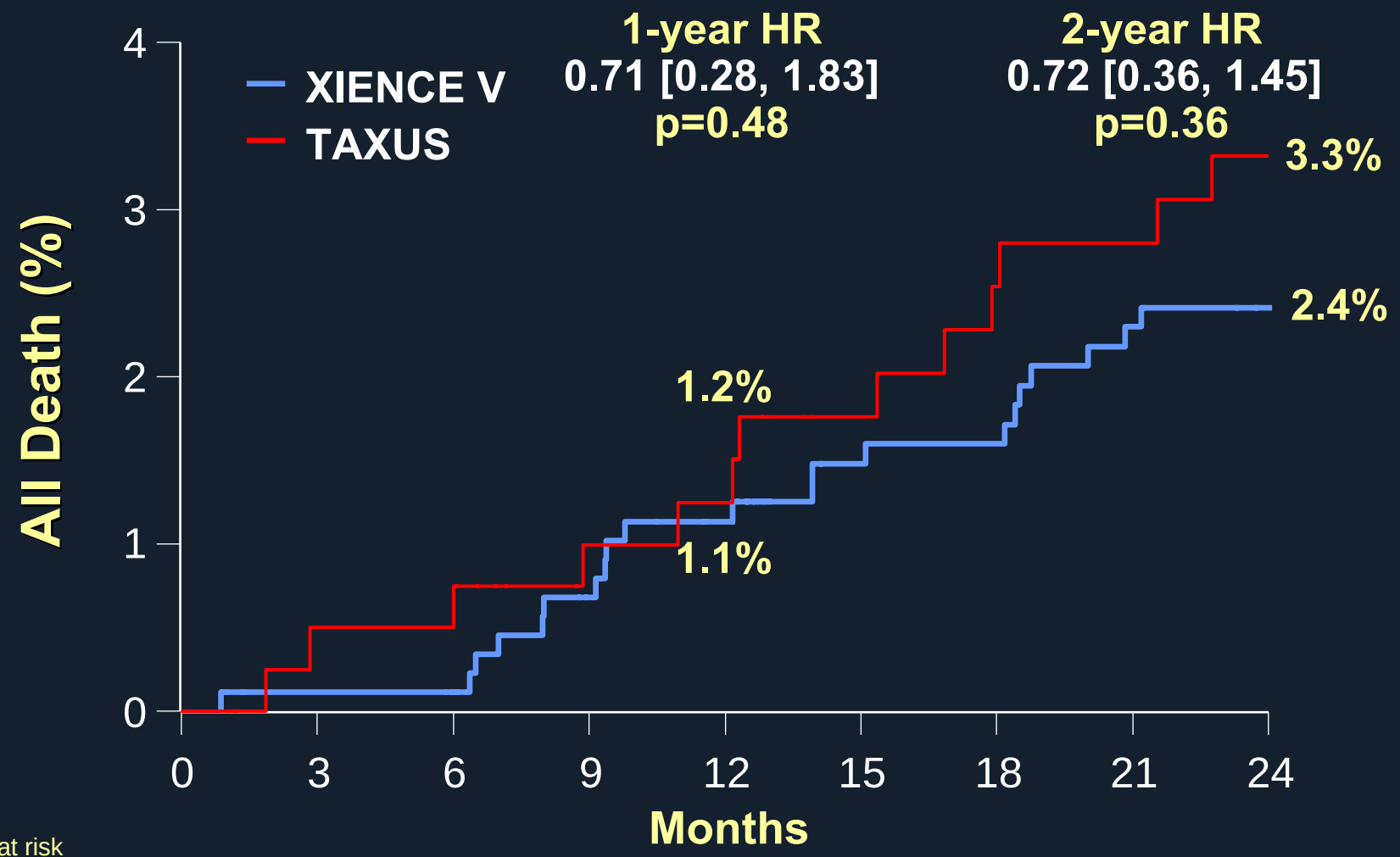
SPIRIT II + III: All Death



Number at risk									
XIENCE V	892	885	881	873	865	845	844	836	834
TAXUS	409	401	399	393	387	377	373	373	371

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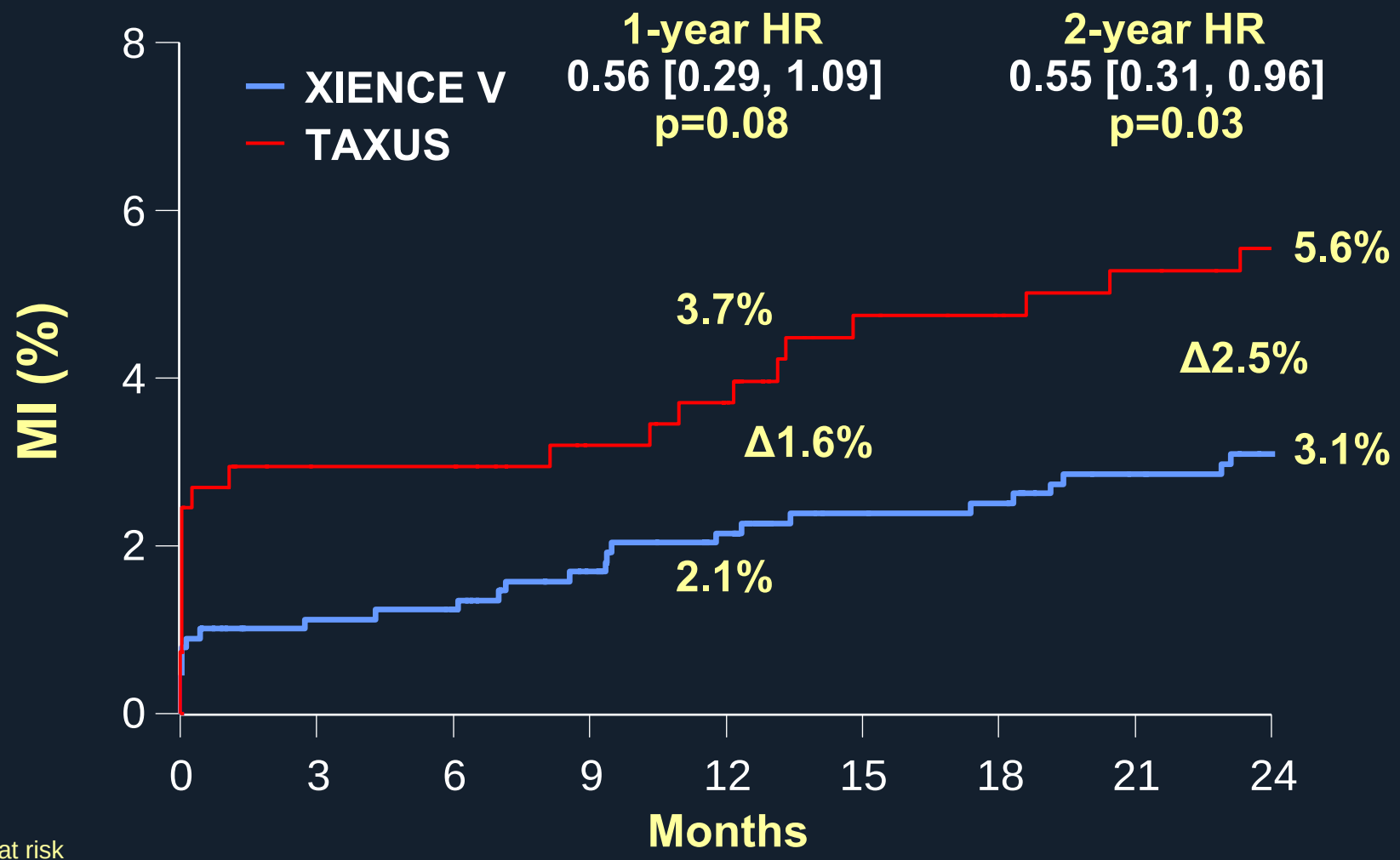
SPIRIT II + III: Myocardial Infarction



Number at risk									
XIENCE V	892	876	871	859	848	826	824	814	810
TAXUS	409	390	388	381	375	361	357	355	352

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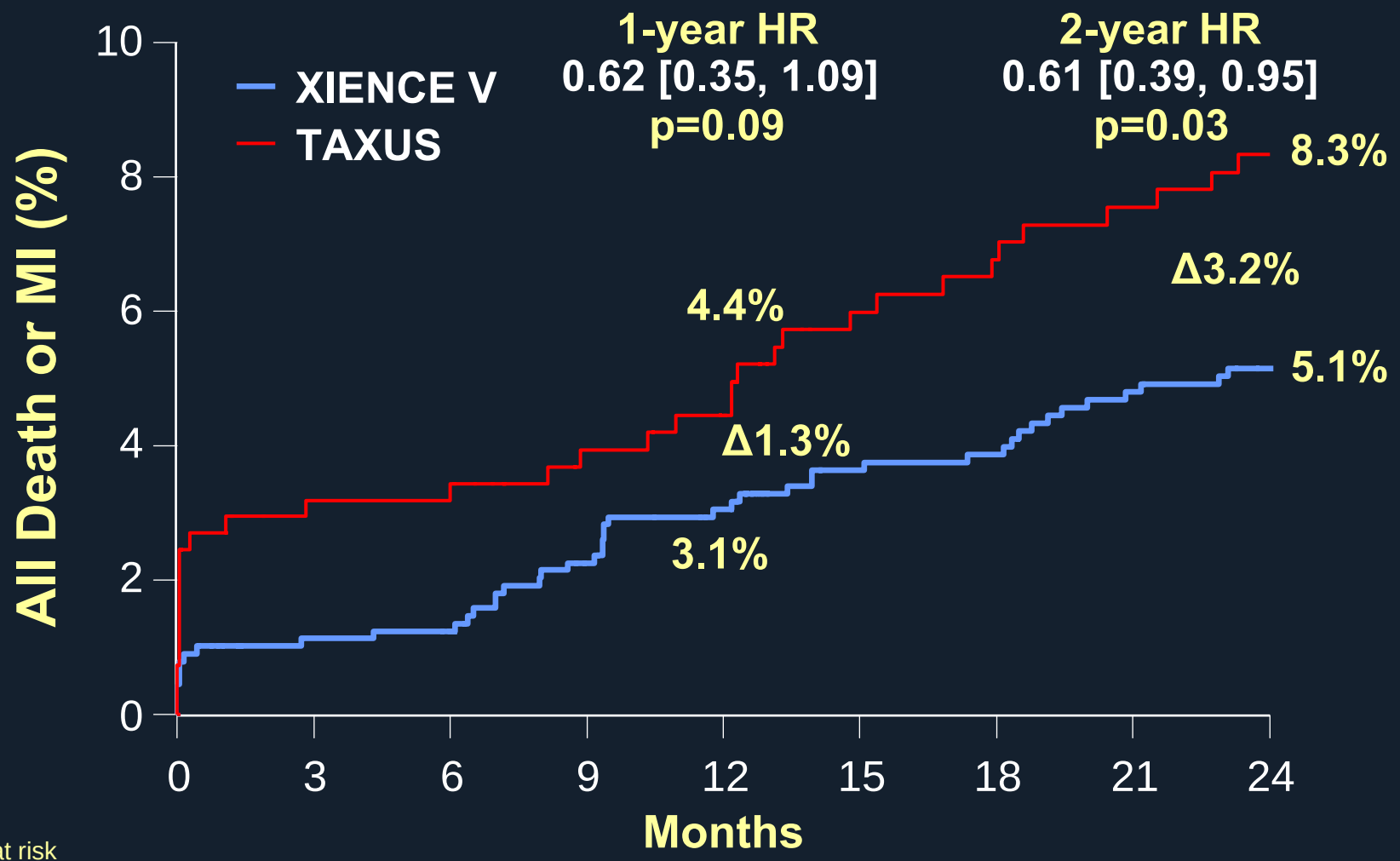
SPIRIT II + III: Death or MI



Number at risk									
XIENCE V	892	876	871	859	848	826	824	814	810
TAXUS	409	390	388	381	375	361	357	355	352

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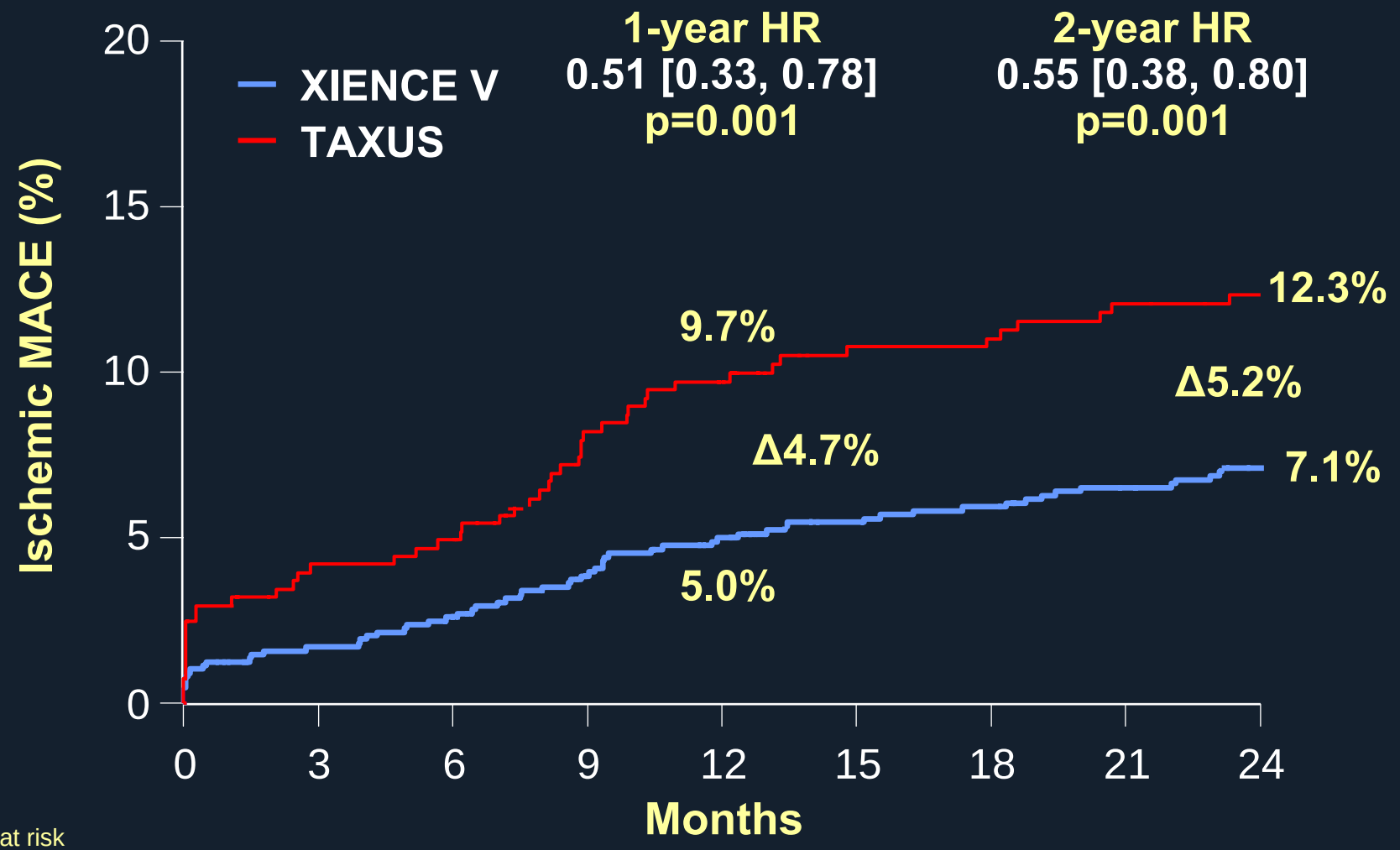
SPIRIT II + III: Ischemic MACE



Number at risk									
XIENCE V	892	871	859	841	827	804	800	790	783
TAXUS	409	386	381	363	354	340	335	332	329

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MACE = Cardiac death, MI, or ischemic TLR

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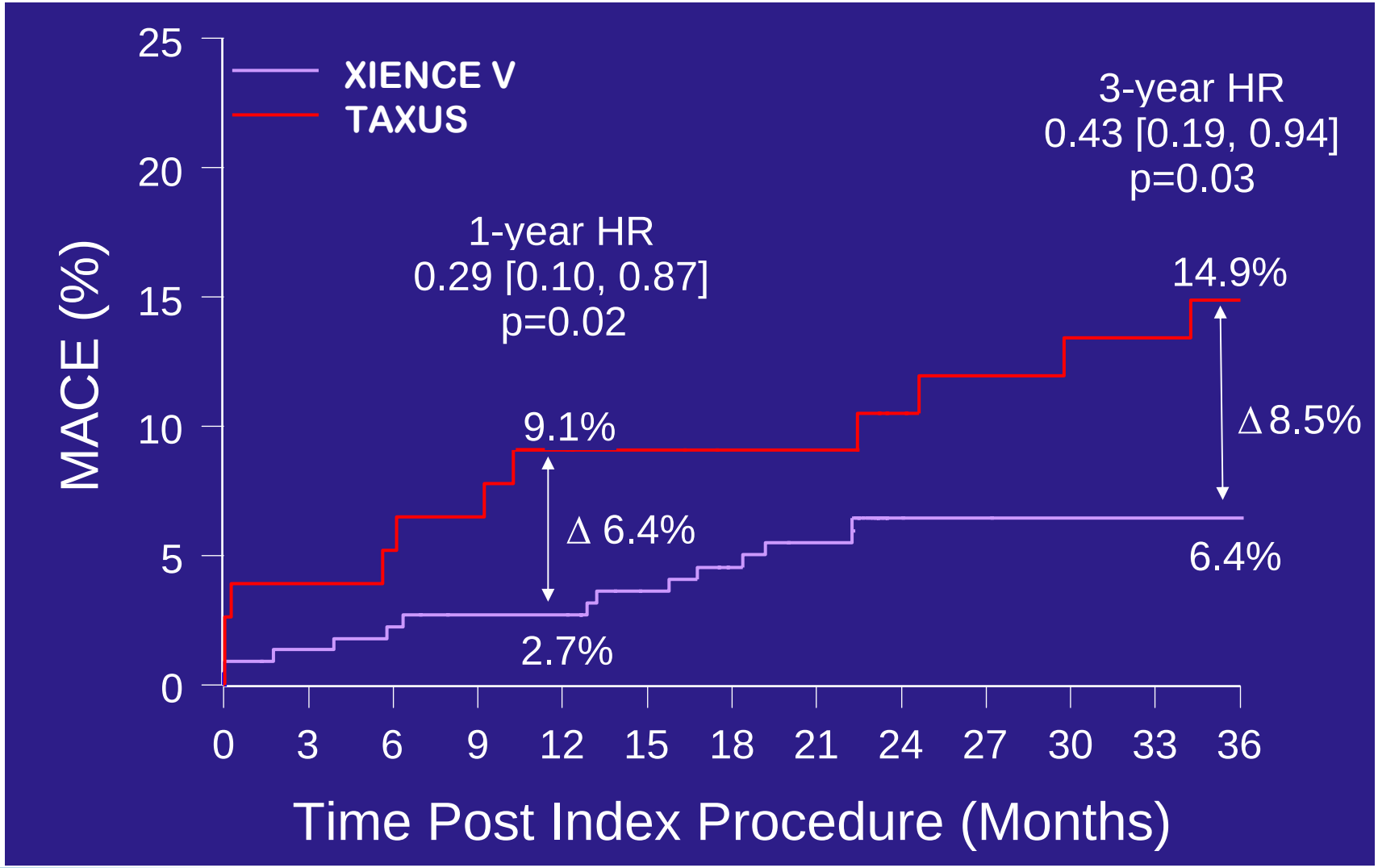
Cumulative Incidence Rates of MACE

Spirit II



Serruys PW. ACC 2009.

Spirit

SPIRIT IV Trial

>1000 randomized diabetics

Randomized (N=3,690)

2 | 1

XIENCE V (N=2,460)

TAXUS (N=1,230)

Single blind
No angiographic FU

Up to 3 lesions in 1, 2 or 3 separate vessels (2 max per vessel)

Primary endpoint: MACE at 12 months

(cardiac death, MI, ischemia-driven TLR)

Primary Endpoint Results

TCT September 2009

San Francisco

TCT 2009

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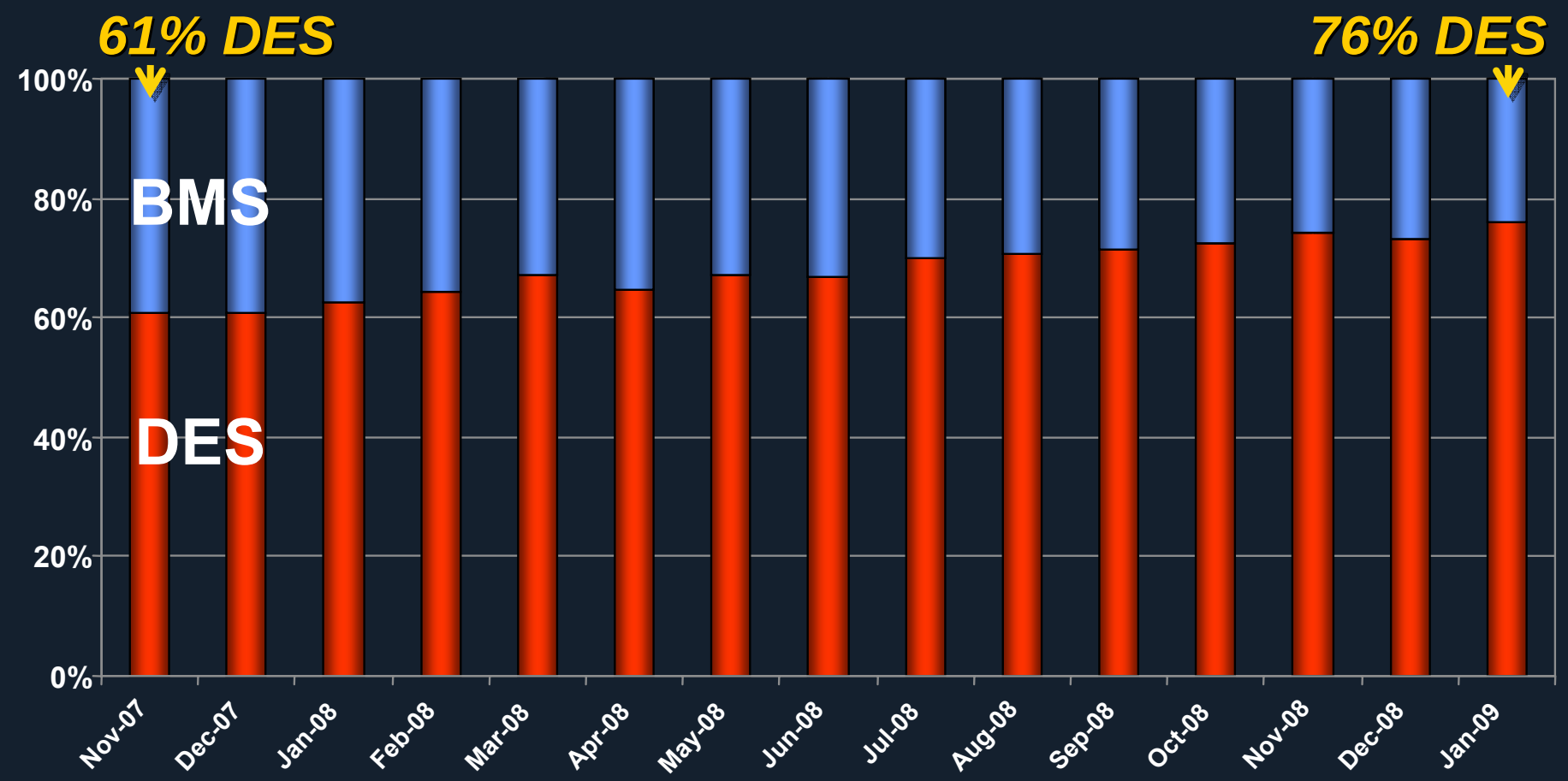
US BMS/DES Penetration

November 2007 – January 2009



Sources: MRG Marketrack, MDT, ABT, BSX and JNJ

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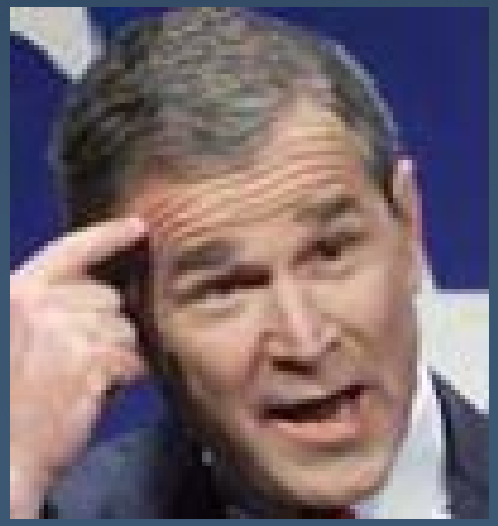
NewYork-Presbyterian
The University Hospital of Columbia and Cornell

Examining all the current data objectively supports the belief that 1st generation DES are safe and effective in a broad cross section of pts. And 2nd generation DES may be safer and more effective!



"I think we all agree, the past is over."

George W. Bush
(Ex) President of the U.S.