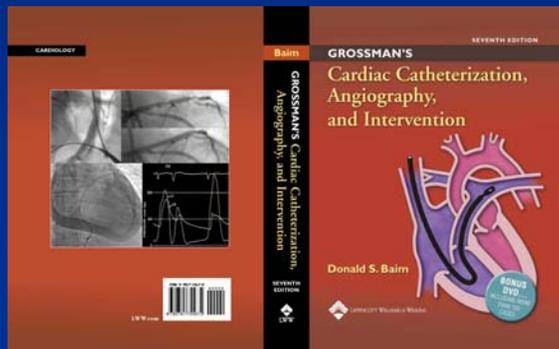


FDA Panel on Drug-eluting Stent Safety
December 7 and 8th, 2006

Boston Scientific Presentation: Part I
On-label Use of the TAXUS[®] Drug-eluting Stent System

Donald S. Baim, M.D.
Executive Vice President
Chief Medical and Scientific Officer
Boston Scientific Corporation

Donald S. Baim, MD



Faculty member since 1981
Professor of Medicine, 1994-2006

Founder and Chief
Interventional Cardiology Section 1981-2000

Senior Physician
Interventional Cardiologist 2000-2006

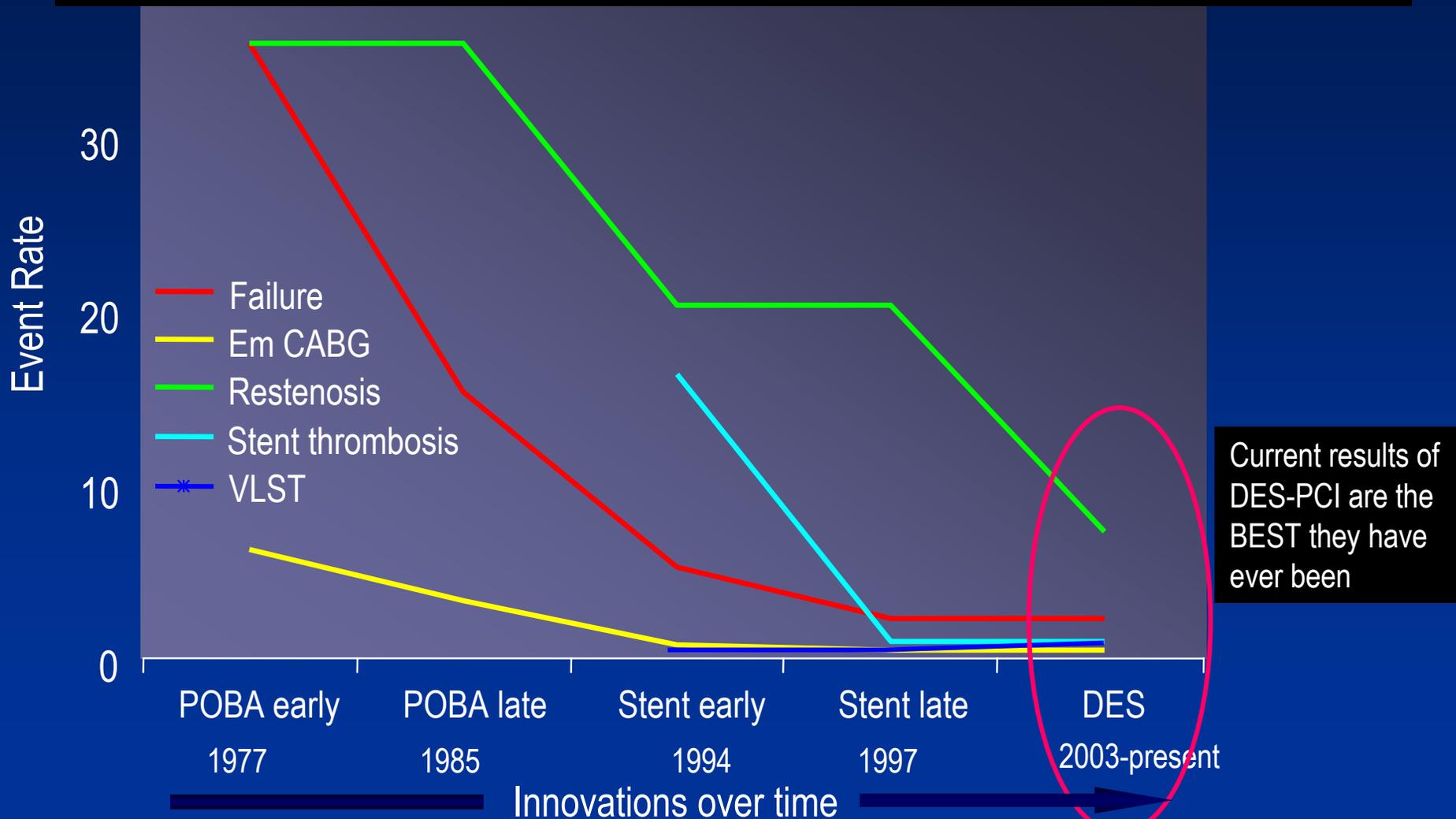
Co-founder (with Dr. Kuntz)
Chief Scientific Officer
Harvard Clinical Research Institute

Editor-in-Chief, (4th through 7th edition [2006])
*Grossman's Cardiac Catheterization,
Angiography and Intervention*

Now (July 1, 2006) Executive Vice President
Chief Medical and Scientific Officer
Boston Scientific Corporation

Evolution of PCI: The dominant coronary revascularization since 1990

Over the last 30 years, percutaneous coronary intervention (PCI) has undergone progressive improvements in success, safety, and durability, as serial new technologies have been launched. While each innovation solved a serious prior problem, it has sometimes introduced rare new adverse events (e.g., in-stent restenosis, stent thrombosis).



Current results of DES-PCI are the BEST they have ever been

TAXUS® SR Stent Randomized Clinical Data

The Taxus I, II, IV, and V randomized trials compared the TAXUS® Slow-Release (SR) Stent to Bare Metal Stent (BMS) controls in 2,797 patients, median 4 year follow-up:

- a PROFOUND *clinical benefit* reduction in repeat revasc. ($\Delta - 9.7\%$, or 48 % relative)
- with trends towards LESS Death ($\Delta -0.3\%$) or Q-MI ($\Delta -0.1\%$) through last follow-up

This favorable risk benefit was seen in all studied sub-groups, with TLR reductions of :

- Diabetics (n=715) $\Delta - 11.5\%$, (46% relative), $p < 0.0001$
- Small vessels ($\leq 2.5\text{mm}$) (n=965) $\Delta - 13.2\%$, (48% relative), $p < 0.0001$
- Long Lesions $\geq 28\text{ mm}$ (n=341) $\Delta - 18.2\%$, (58% relative), $p < 0.0001$
- Multiple Stents/vessel (n=497) $\Delta - 23.1\%$, (64% relative), $p < 0.0001$

Stent thrombosis rates were not statistically different from the BMS Control for either :

	<u>4 years cum.</u>	or	<u>beyond 1 year (VLST)</u>
per protocol	1.3 vs. 0.8 %		$\Delta +0.4\%$, $p = 0.057$
ARC 1 ^o def.+prob.	1.8 vs. 1.1 %		$\Delta +0.5\%$, $p = 0.081$
ARC Total	3.5 vs. 3.6 %		$\Delta - 0.1\%$, $p = 0.786$

Plavix use beyond 6 months with TAXUS showed a trend towards reduced Death or MI

Agenda

Background

Stent Thrombosis – ARC Definitions

TAXUS Meta-Analysis – All Patients

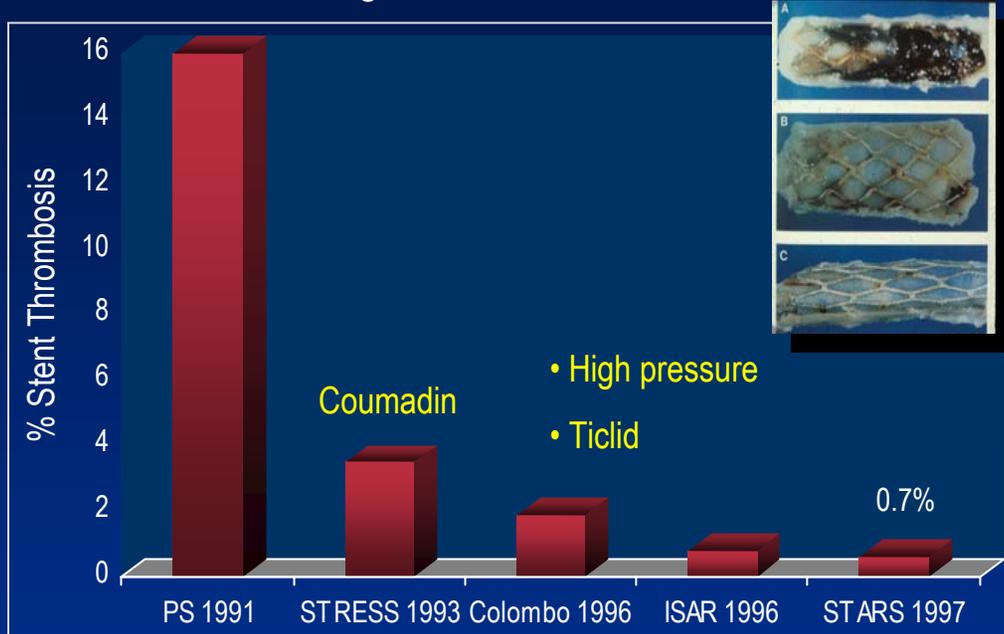
TAXUS Meta-Analysis – Subgroups

Antiplatelet Usage

Summary and Conclusions

A Brief History of Stent Thrombosis

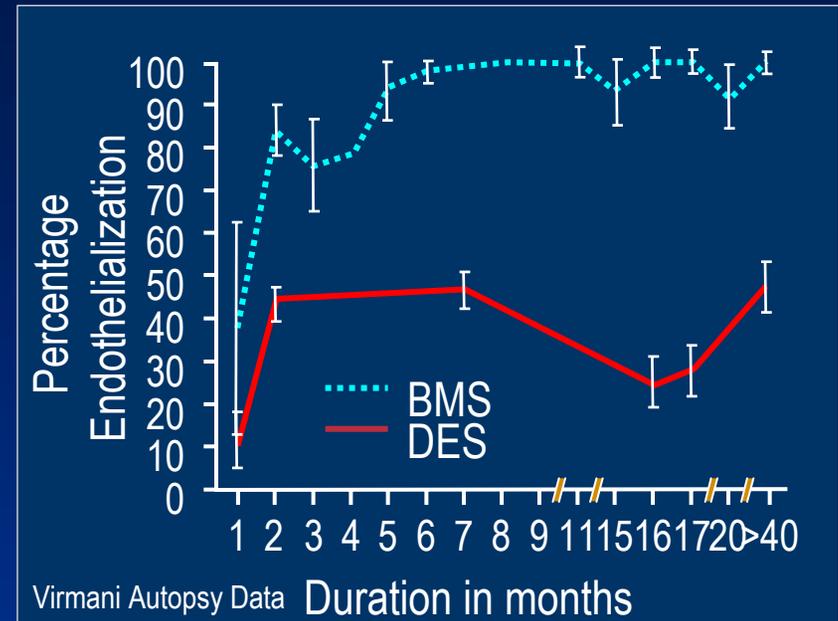
Decreasing incidence of ST with BMS



Stent thrombosis with BMS decreased progressively due to the use of high-pressure stent deployment and 1 month of dual anti-platelet Rx (aspirin, and ticlopidine or clopidogrel).

SAT almost always occurred within 1 month of implantation.

Incomplete/delayed endothelial coverage with DES



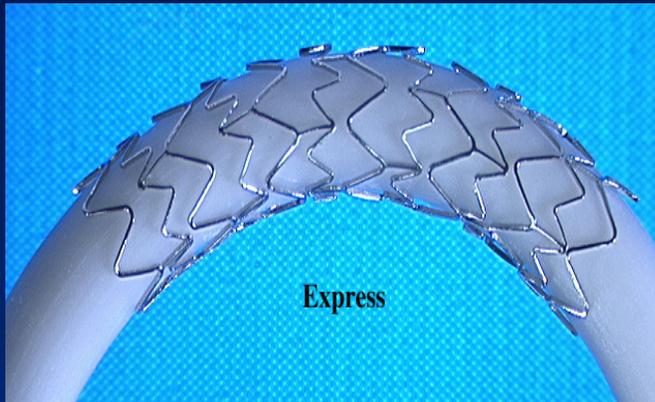
While the main benefit of DES (↓ in-stent tissue) has decreased restenosis, the associated drugs or polymers may interfere with rapid complete endothelial coverage, at least in some patients



Delayed endothelialization of DES was anticipated, as shown by longer (3 – 6 months) anti-platelet therapy, but it *may* have unmasked a new (but rare, ~ 0.5%) event : Very Late ST > 1 year after implantation.

The TAXUS[®] Express[®] Stent – Boston Scientific Corporation

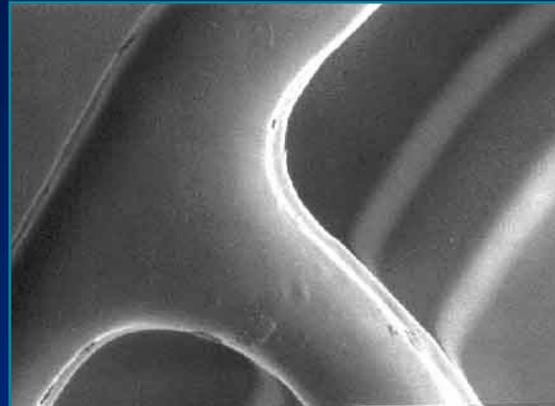
Stent



Express[®]

Stainless steel Tandem
Architecture[™] Stent Design
Maverick[®] Balloon Catheter
Flexible, deliverable

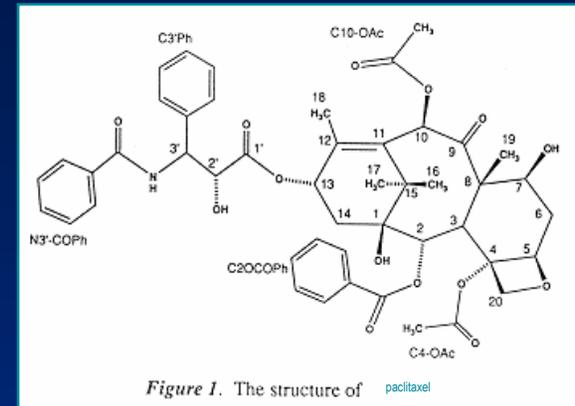
Polymer



Translute[™]

ABA triblock thermoplastic elastomer
Styrene- b isobutylene- b styrene
biostable and biocompatible
provides controlled matrix release

Drug



Paclitaxel

Binds tubulin
Stabilizes microtubular
deconstruction
Suppresses migration and
proliferation (cytostatic) at low
concentrations

Studied clinically in 2 different versions:

• Slow-release (SR)

– commercialized version

• Moderate release (MR)

– roughly 3x released dose compared to SR

-- never commercialized in any country

DES Trials and Follow-up

Currently, only TAXUS® and Cypher® stents have enough patients with enough long-term follow-up to accurately assess VLST and late clinical events



The TAXUS[®] SR Stent Trials (N = 2,797)

Patients randomized to Taxus SR vs BMS



Cohort 1 (SR)

Stent Platform	 NiRx™	 NiRx™	 Express	 Express ²
Study Objective	Safety and feasibility	Efficacy, dose-response	Pivotal	Indication expansion
n = ITT patients	61	266	1,314	1,156
1° endpoint	Safety and procedural success	% net volume obstruction (IVUS)	TVR Non-TVR	TVR Non-TVR
Long-term F/U available	5 years	4 years	4 years	2 years
RVD* (mm)	3.0 -3.5	3.0 -3.5	2.5 -3.75	<u>2.25</u> -4.0
Lesion	Single	Single	Single	Multiple overlap
Lesion length* (mm)	≤12	10 -12	10 - 28	10 - <u>46</u>
Max. # planned study stents per lesion/patient	1	1	2	2

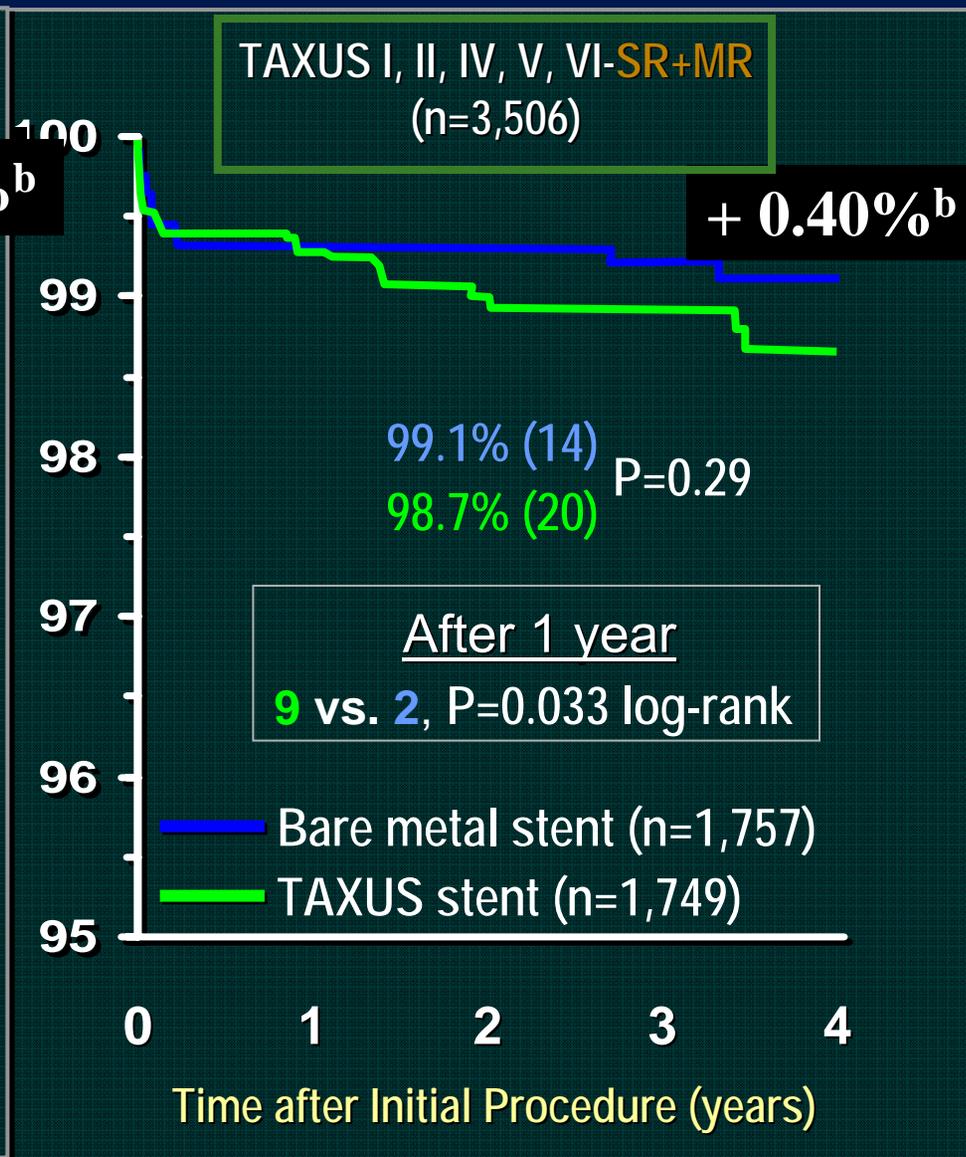
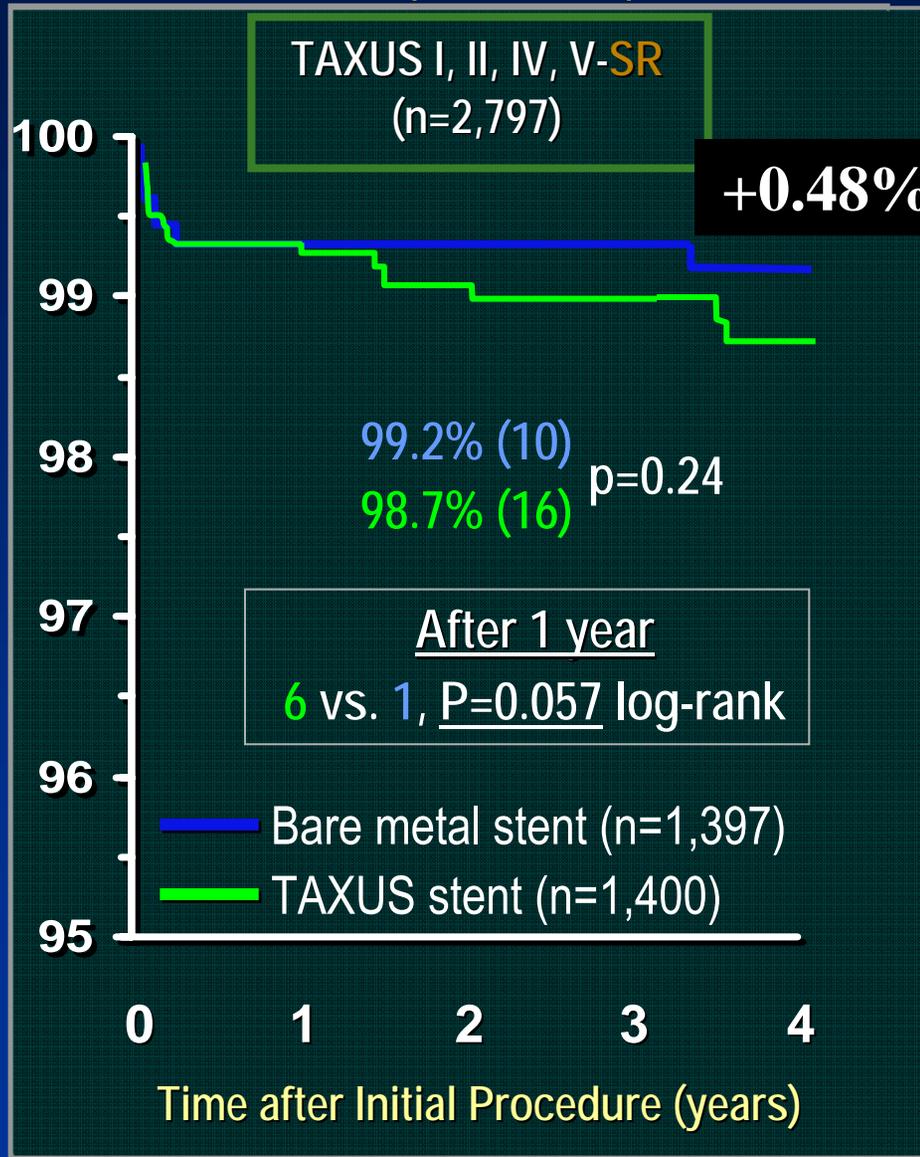
RVD=Reference Vessel Diameter; * As per trial inclusion/ exclusion criteria

NiRx is a trademark of Medinol, Ltd., Jerusalem, Israel

Methodology

- Pilot, pivotal and label extension randomized trials (IDE)
- Full monitoring and FDA audits of source data
- Independent Core Laboratories (angio, IVUS, EKG)
- Outside adjudication of all endpoints
 - HCRI for ARC stent thrombosis adjudication
- Internal (Boston Scientific) data entry and analysis
- Independent review and analysis of all patient-level data
 - ✓ Pocock Global Data and Safety Monitoring (October 2006)
 - ✓ Cardiovascular Research Foundation (November 2006)
 - Serruys (pending)

Independent CRF patient-level meta-analysis Freedom From (Protocol) Stent Thrombosis



a. Difference = BMS – Cypher

b. Difference = BMS – Taxus

Agenda

Background

Stent Thrombosis – ARC Definitions

TAXUS Meta-Analysis – All Patients

TAXUS Meta-Analysis – Subgroups

Antiplatelet Usage

Summary and Conclusions

ARC Definitions – a large and needed step towards clarity

Definite/Confirmed

Acute coronary syndrome AND [either
Angiographic confirmation of thrombus or occlusion
OR
Pathologic confirmation of acute thrombosis]

Probable

Unexplained death within 30 days
OR

Target vessel MI, [even] without angiographic confirmation of
thrombosis or other identified culprit lesion

Possible

Unexplained death after 30 days

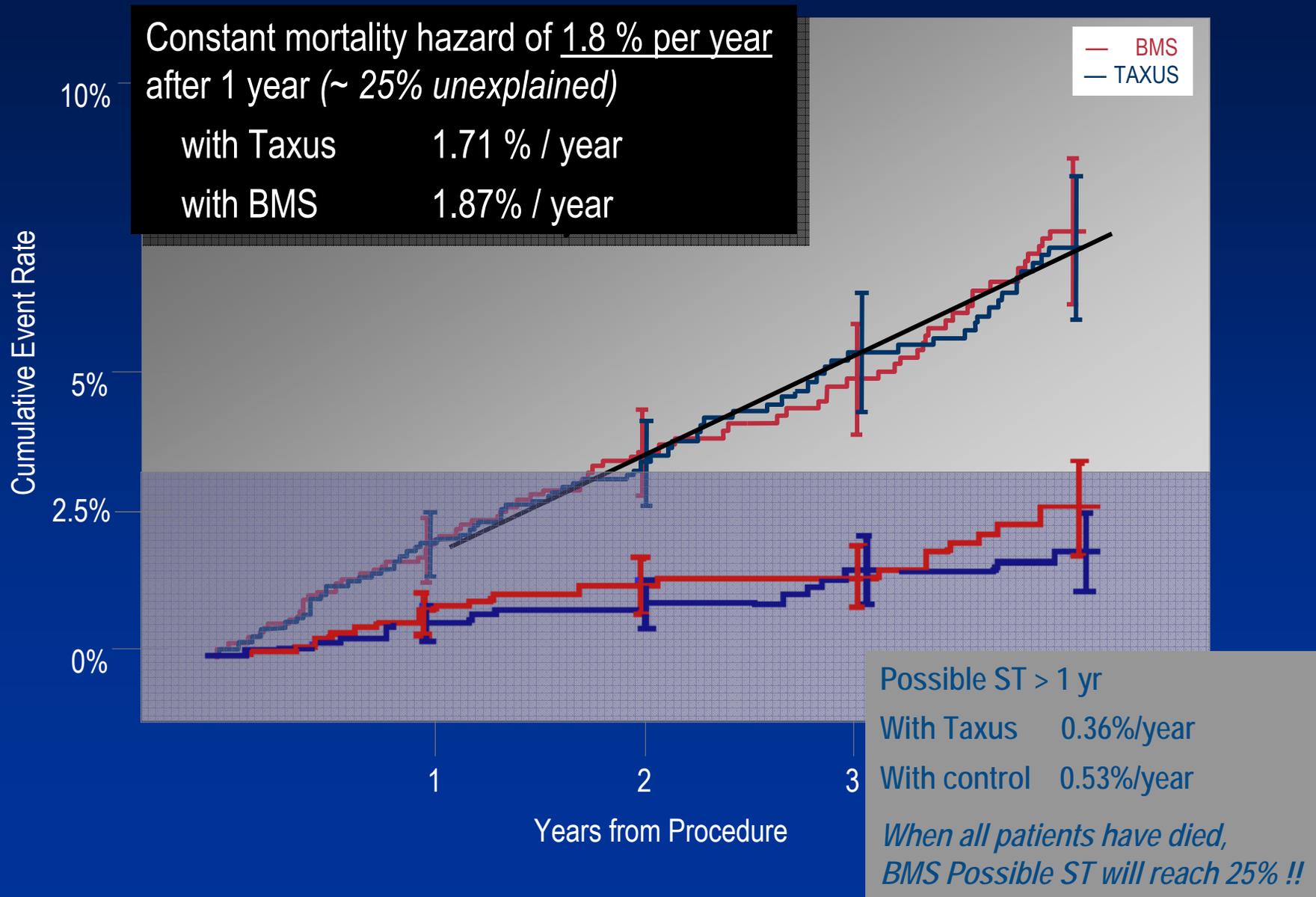
ARC Definition (not a single definition, but a set of definitions)

	Primary (TLR censored)	Total (post-TLR retained)
Definite	Too Narrow <i>(specific, but not sensitive and may miss adverse events)</i>	Too Broad
Definite + Probable*	Best Balance* <i>(optimal sensitivity and specificity best suited for examining any differential ST mechanism)</i>	Too Broad
Definite + Probable+ Possible	Too Broad <i>(sensitive, but not specific and may dilute out any true safety signal)</i>	Too Broad

*Also almost identical to the Protocol definition used in the Taxus trials

Possible Stent Thrombosis is Too Broad

Death in the TAXUS[®] SR Stent Studies (2,797) reflect mostly natural history, and not stent thrombosis



Inclusion of Post-TLR Stent Thrombosis is Too Broad

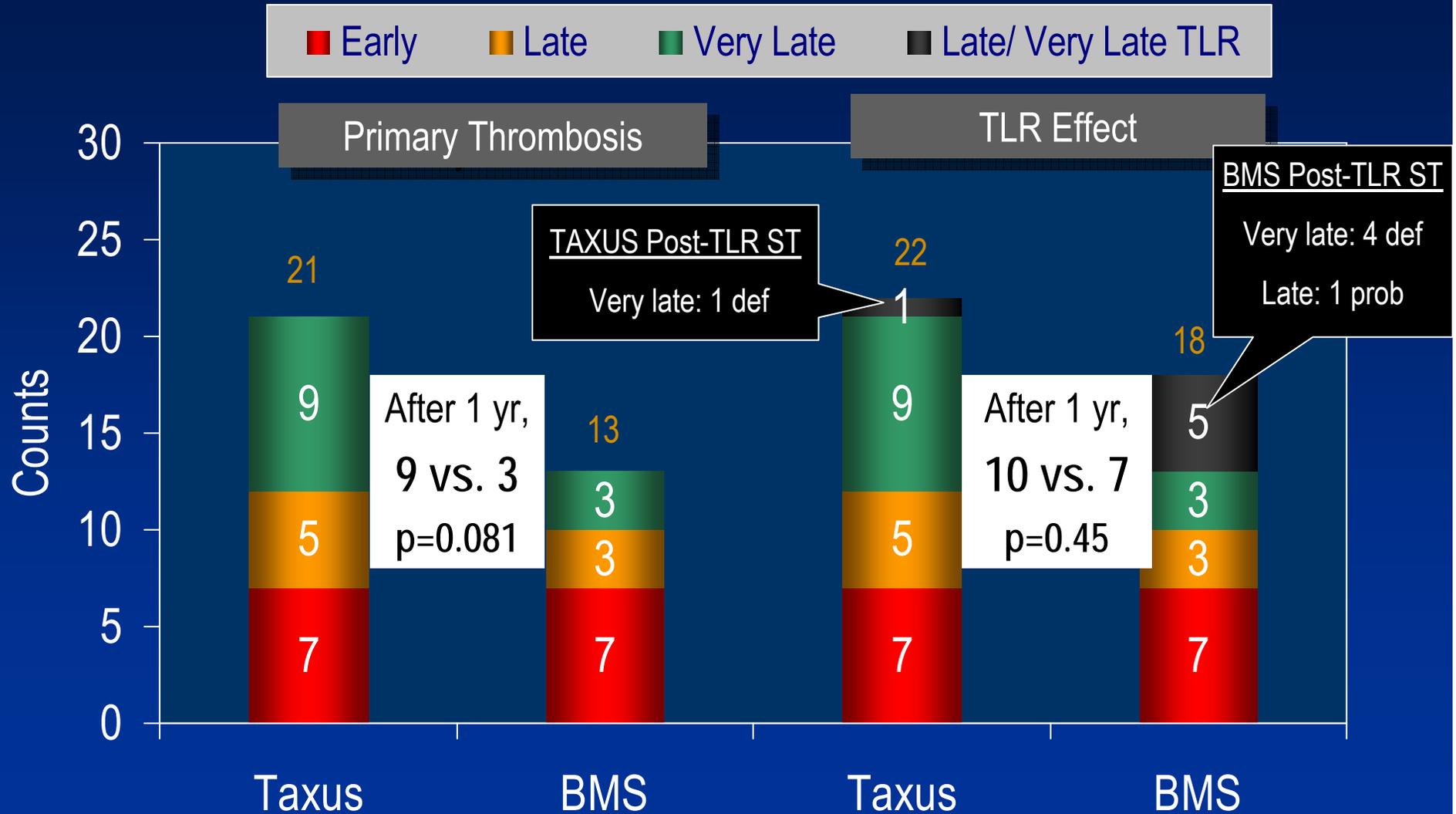
Differential use of post-brachytherapy in BMS arm obscures any mechanistic difference

It is preferable to censor post-TLR thrombosis, and capture any missed events in ITT Death/ MI

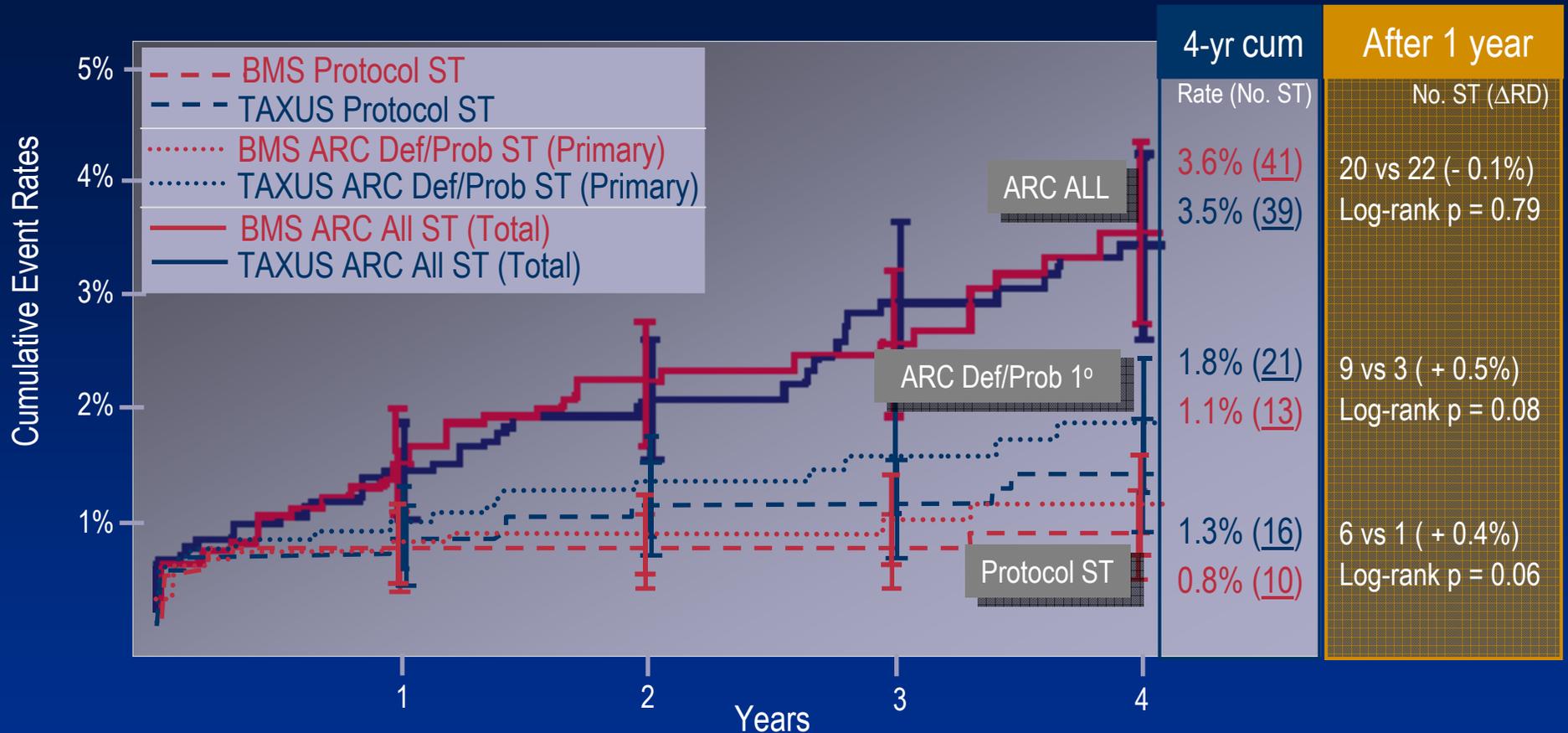
	TAXUS ST (any) N = 39	BMS ST (any) N = 41
Prior TLR	3 / <u>133</u> TLR	8 / <u>266</u> TLR
Time from TLR to ST, mean (min, max)	269 (70, 407)	362 (3, 846)
ST Classification		
Definite/Probable	1	5
Possible	2	3
TLR Procedure	3	8 (7/8 Brachy)
BMS	2	1
PTCA	1	0
Brachytherapy/Atherectomy	0	1
Brachytherapy/PTCA	0	4
Brachytherapy/PTCA/BMS	0	2

ARC Definite/Probable Thrombosis

Inclusion of Prior TLR Events *hinders* (not helps) out understanding of whether any DES increase the Very Late Stent Thrombosis mechanism warrants increased anti-platelet therapy duration !!



Taxus[®] SR Stent has no significant increase in stent thrombosis by *any* definition



	Years	1			2			3			4		
		Prot	Prim	Total									
TAXUS	# Entered	1400	1400	1400	1338	1336	1337	1217	1216	1217	733	730	730
	# Events	10	12	19	4	5	9	0	2	7	2	2	4
BMS	# Entered	1397	1397	1397	1342	1334	1341	1238	1231	1233	750	746	747
	# Events	9	10	20	0	1	10	0	1	3	1	1	8

Agenda

Background

Stent Thrombosis – ARC Definitions

TAXUS Meta-Analysis – All Patients

TAXUS Meta-Analysis – Subgroups

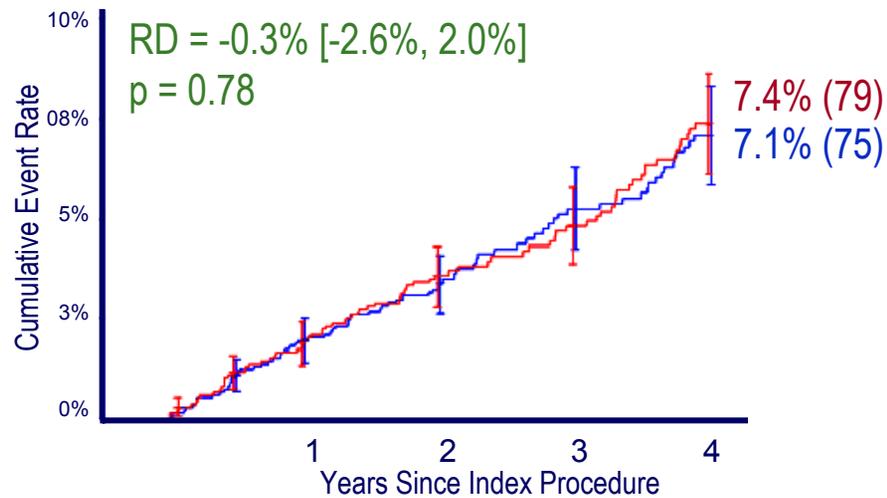
Antiplatelet Usage

Summary and Conclusions

Overall TAXUS[®] Stent Analysis (N = 2,797)

- Sample of Presentation Format

All Death



TAXUS (N=1400)

BMS (N=1397)

RD = Rate Difference = TAXUS — BMS

[95% confidence intervals]

Log-rank p value

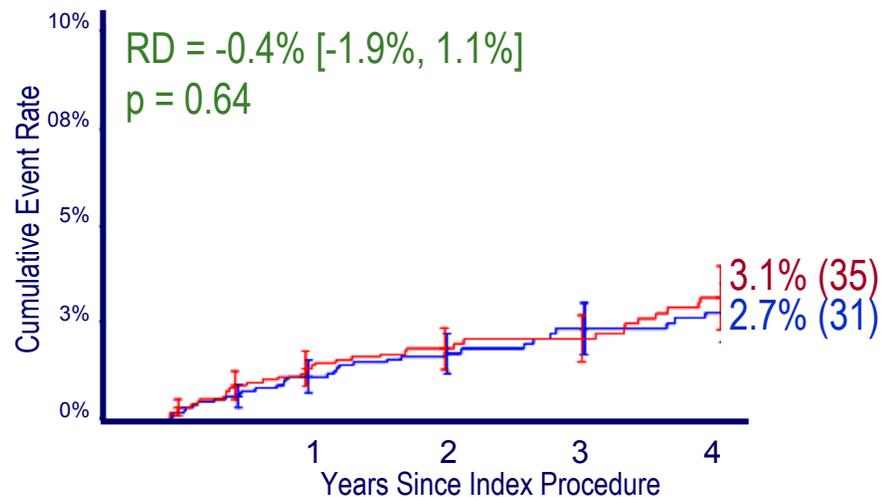
Decrease/ No increase

Increase

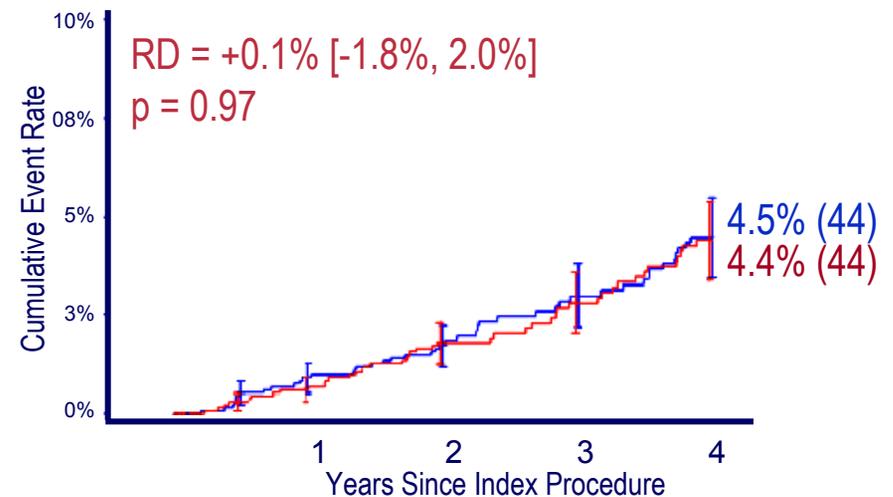
Decrease/No increase

Increase

Cardiac Death



Non- Cardiac Death

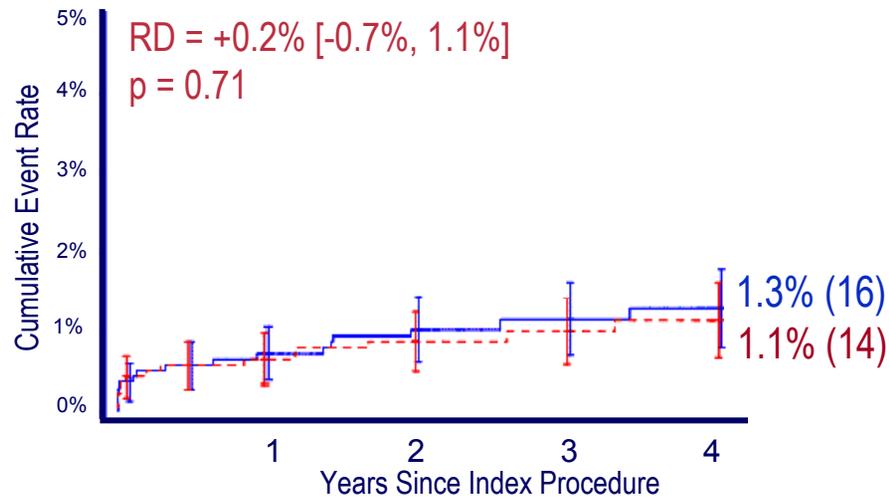


Overall TAXUS[®] Stent Analysis (N = 2,797)

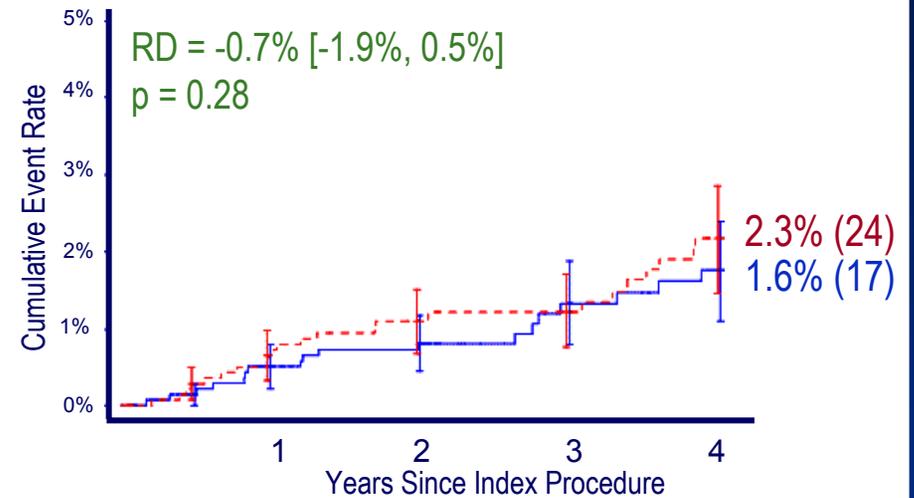
ARC ST (Total = Including post-TLR)

— TAXUS (N=1400) — BMS (N=1397)
 RD = Rate Difference = TAXUS — BMS
No increase Increase

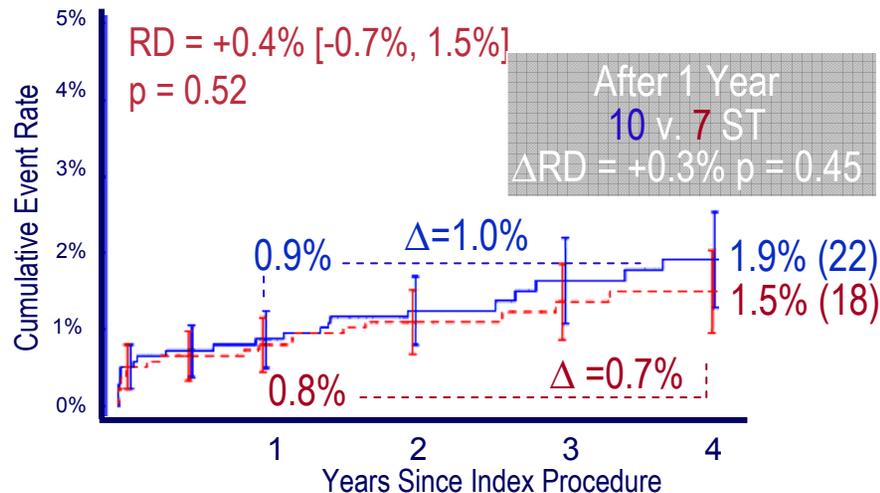
Total Definite ST



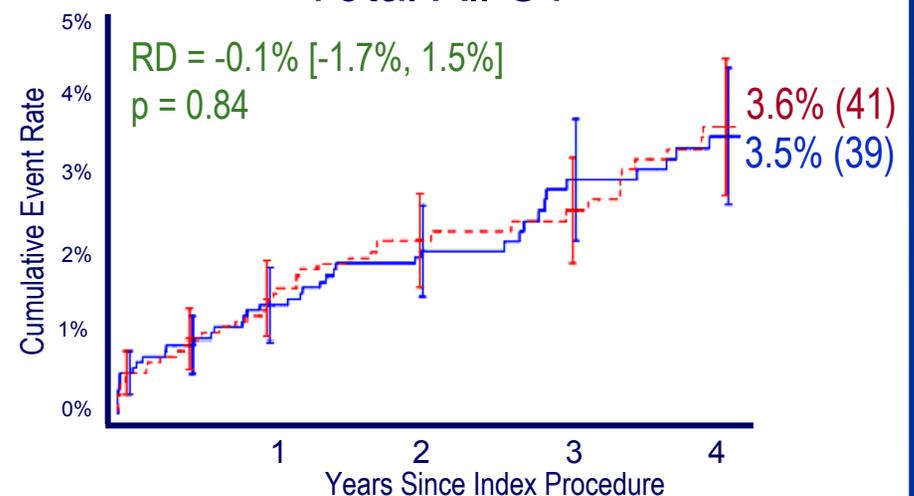
Total Possible ST



Total Definite/Probable ST



Total All ST

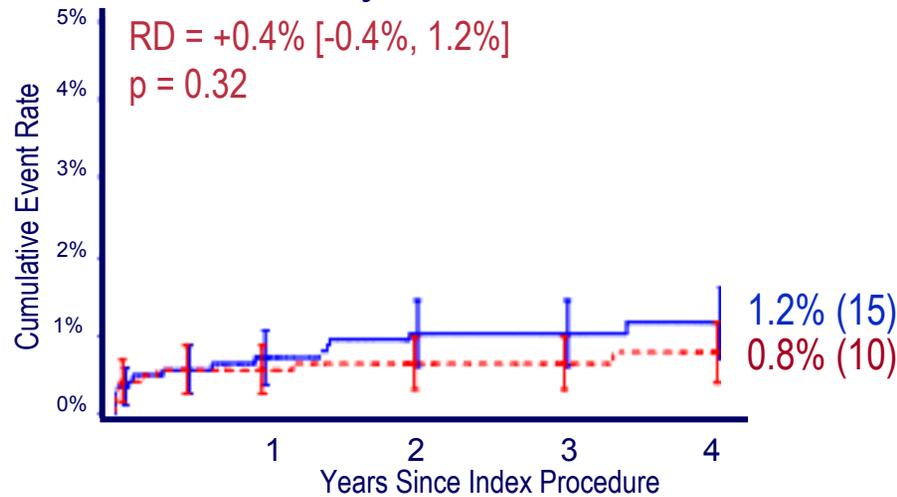


Overall TAXUS[®] Stent Analysis (N = 2,797)

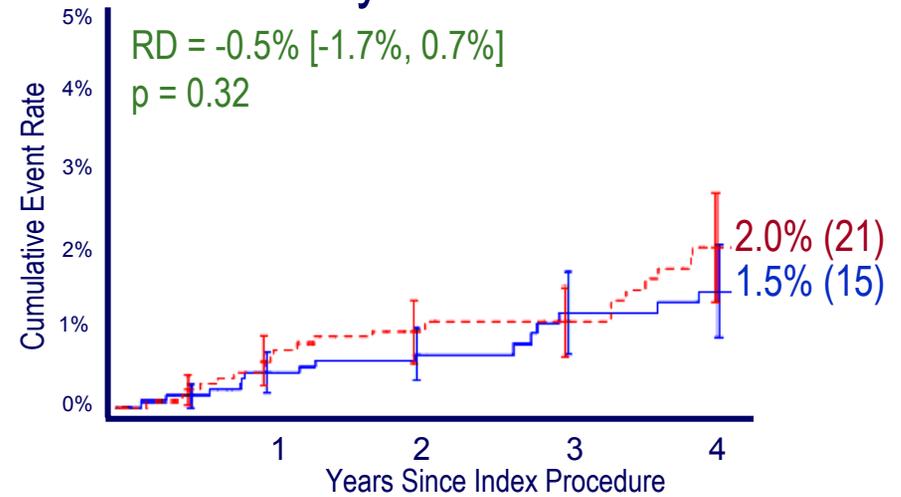
ARC ST (Primary = Censoring ST post-TLR)

— TAXUS (N=1400) — BMS (N=1397)
 RD = Rate Difference = TAXUS — BMS
No increase Increase

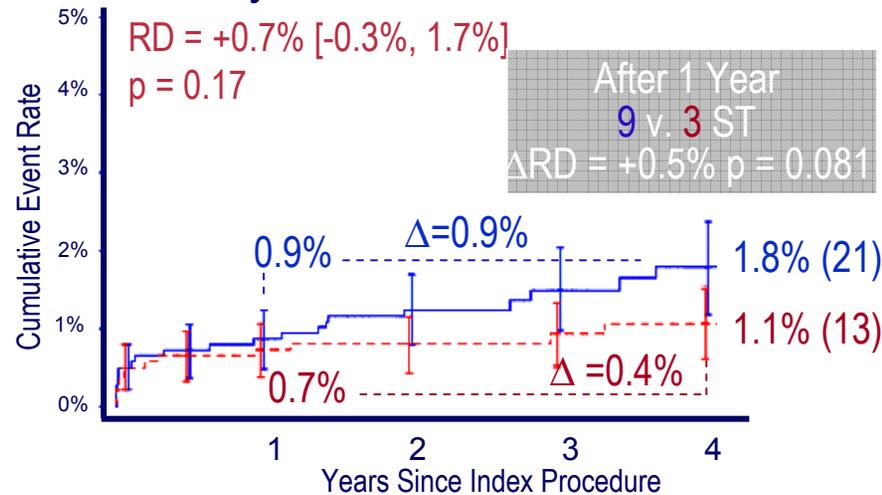
Primary Definite ST



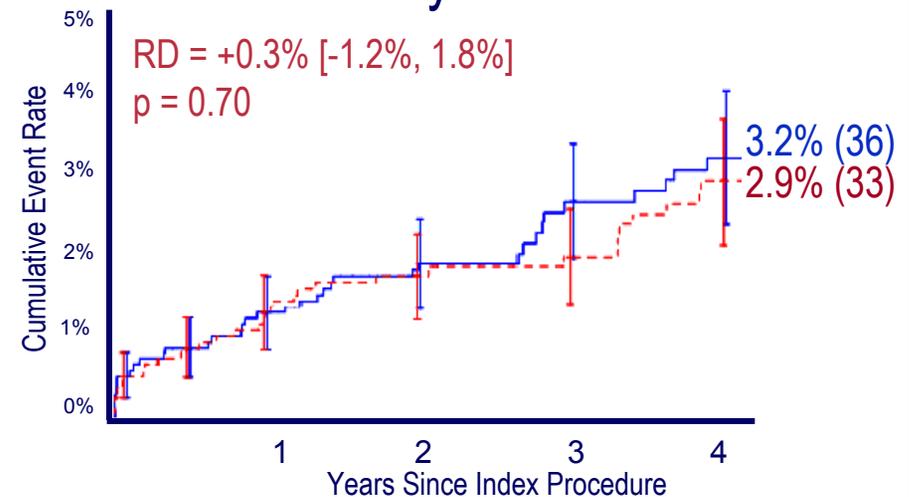
Primary Possible ST



Primary Definite/Probable ST



Primary All ST



But have we spent so much time thinking about the hole,
that we are forgetting about the doughnut?



Late stent thrombosis is just *one*
of several causes of late death
and MI (along with natural history
and restenosis)

Death

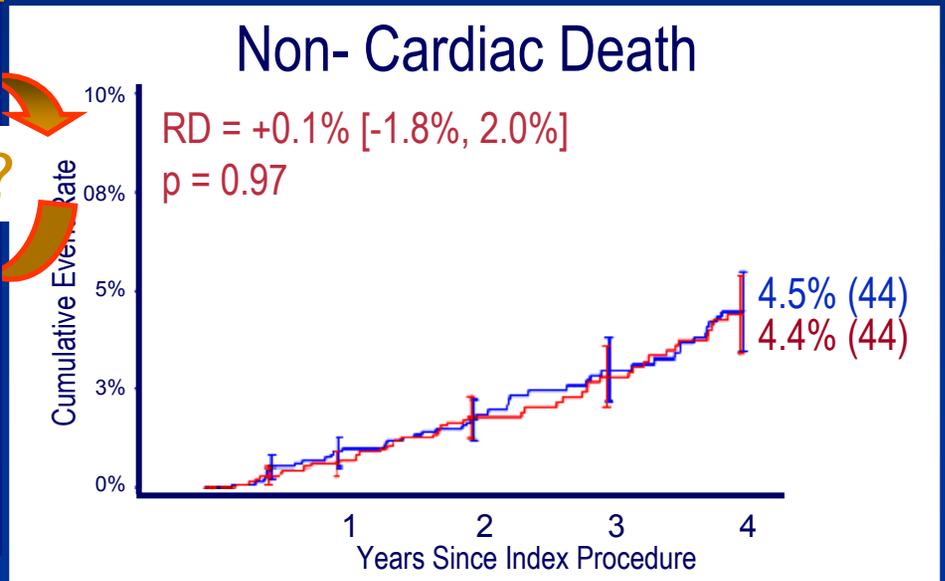
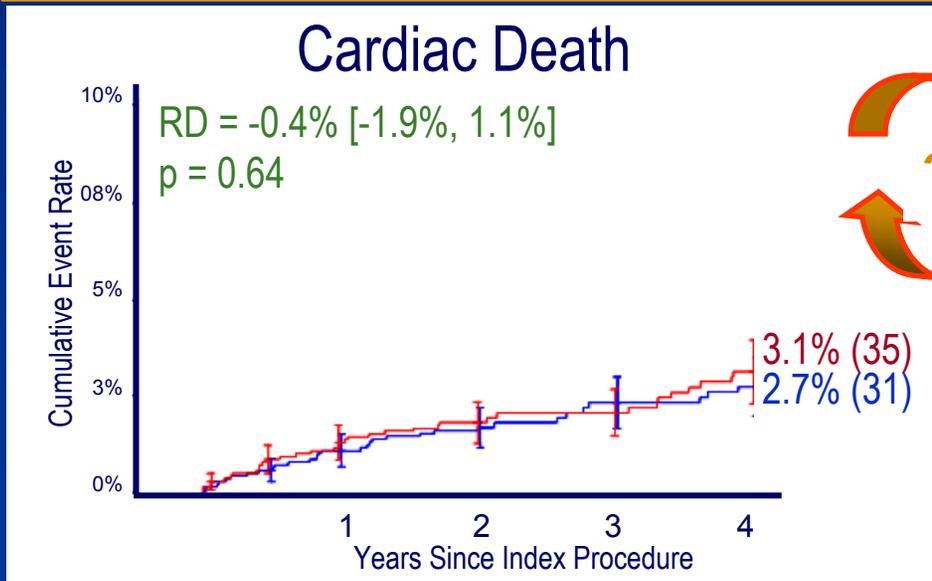
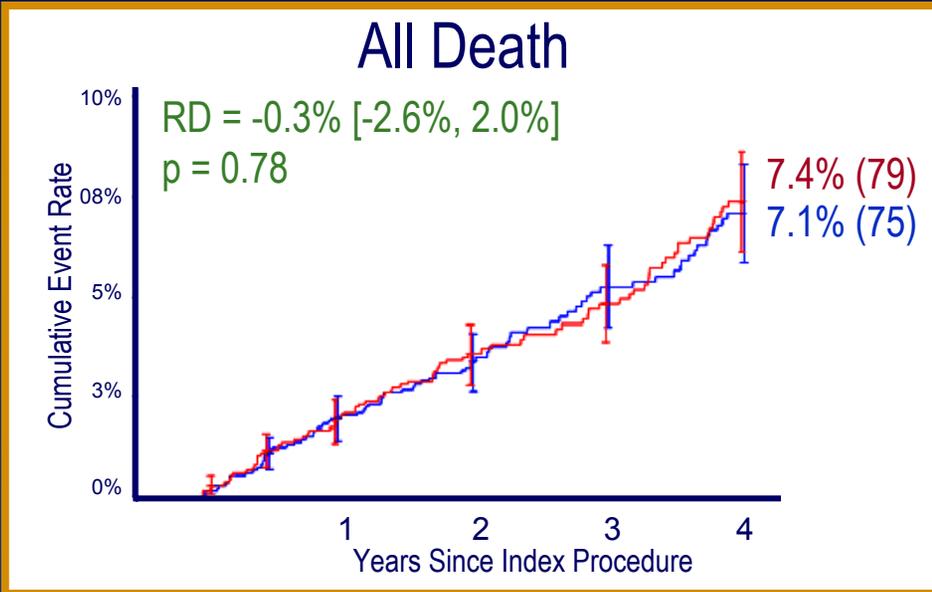
Q-wave MI

Repeat procedures

Overall TAXUS Analysis (N = 2,797)

Death -- Alternative Endpoints

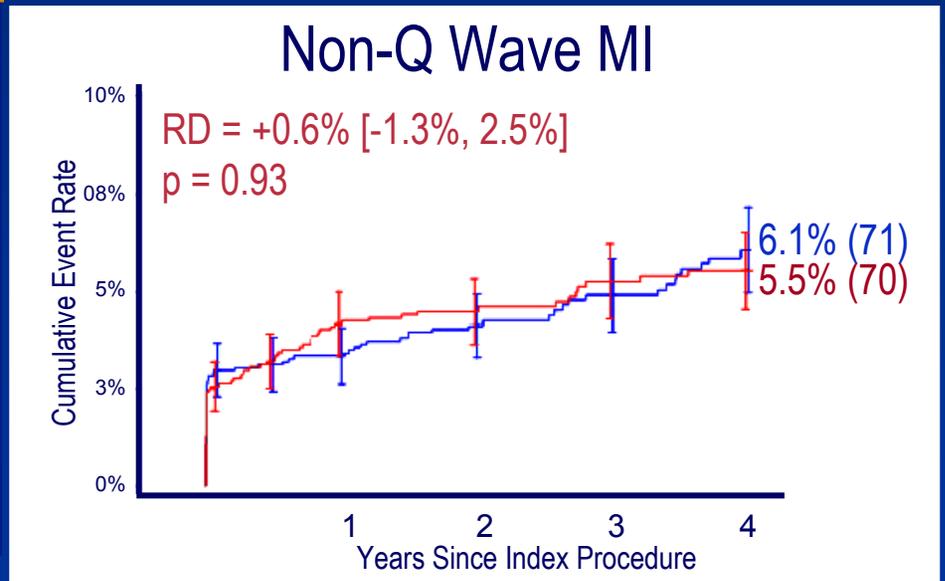
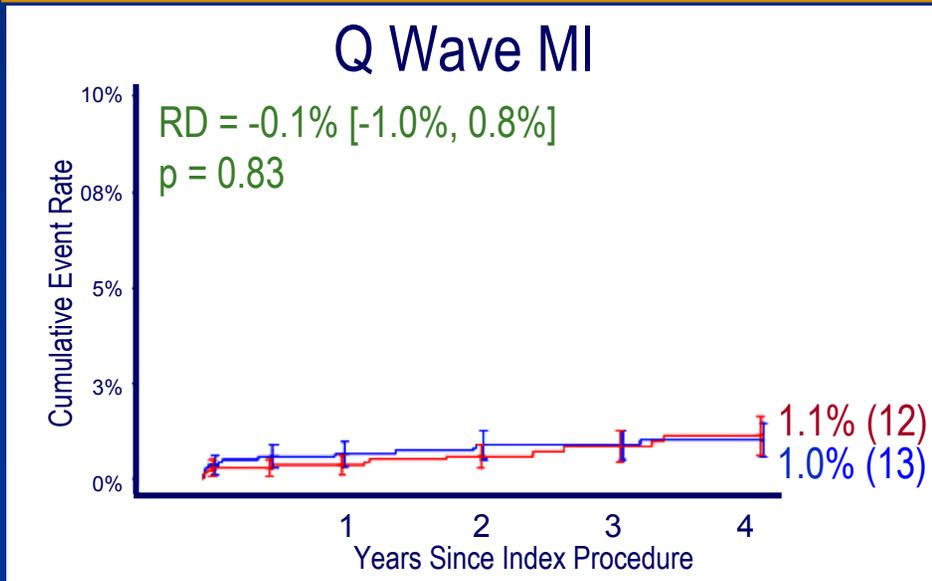
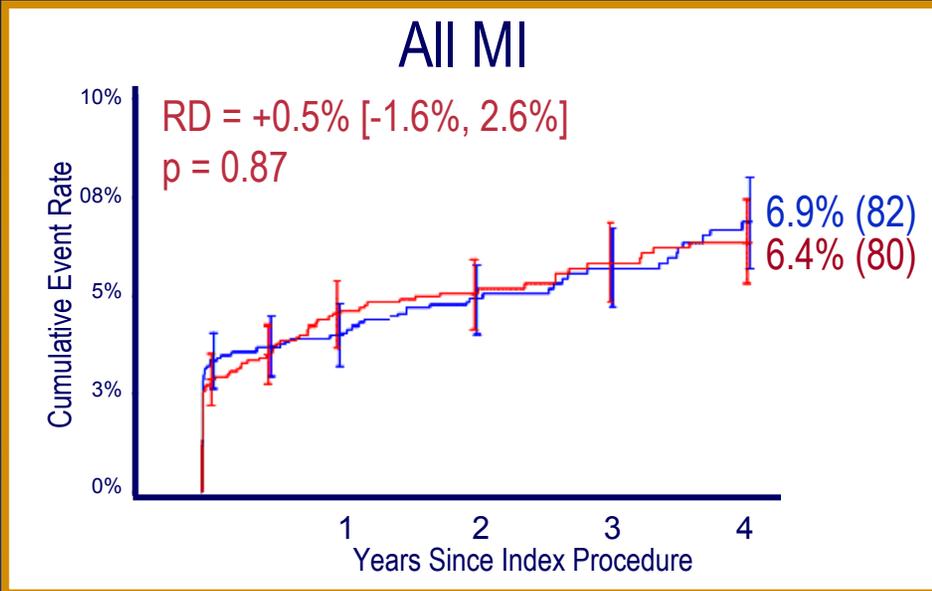
— TAXUS (N=1400) — BMS (N=1397)
 RD = Rate Difference = TAXUS — BMS
No increase Increase



Overall TAXUS[®] Stent Analysis (N = 2,797)

MI -- Alternative Endpoints

— TAXUS (N=1400) — BMS (N=1397)
 RD = Rate Difference = TAXUS — BMS
No increase Increase



Overall TAXUS[®] Stent Analysis (N = 2,797)

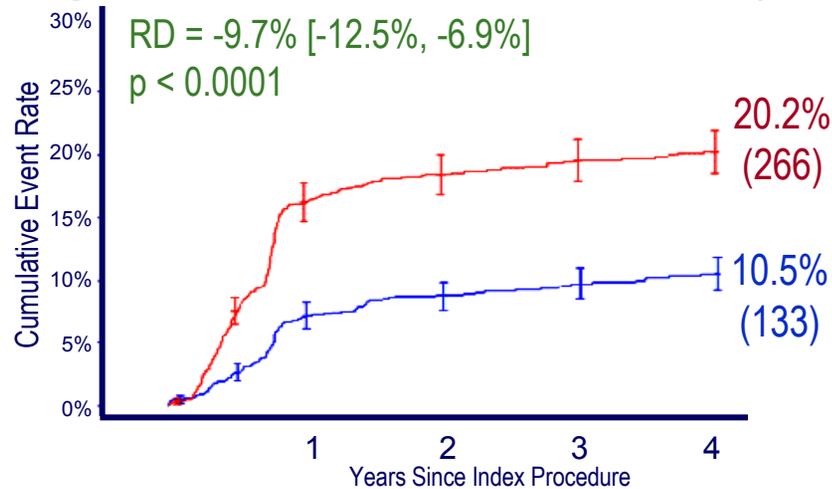
Revascularization

— TAXUS (N=1400) — BMS (N=1397)

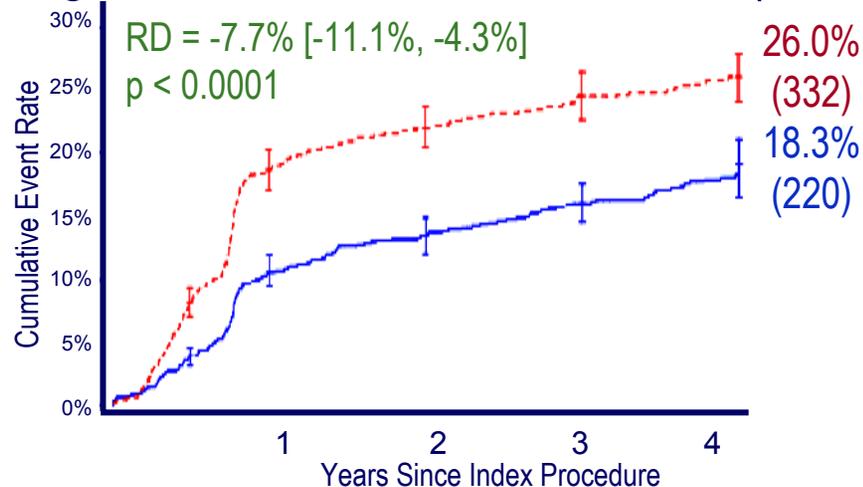
RD = Rate Difference = TAXUS — BMS

No increase Increase

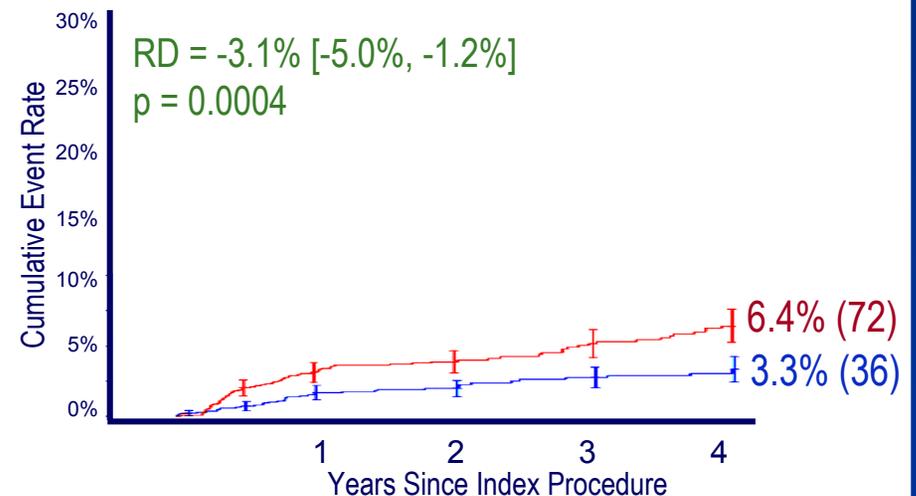
Target Lesion Revascularization (TLR)



Target Vessel Revascularization (TVR)



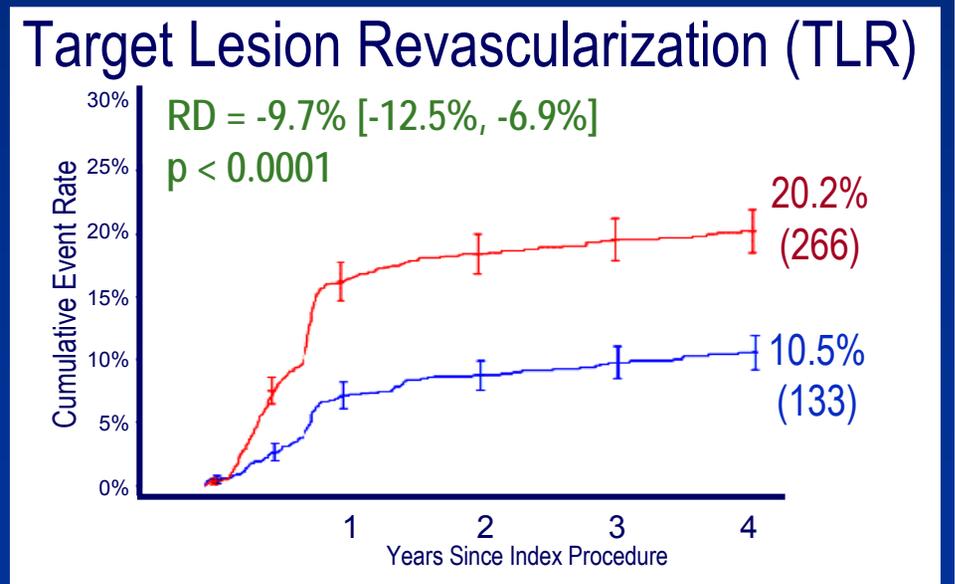
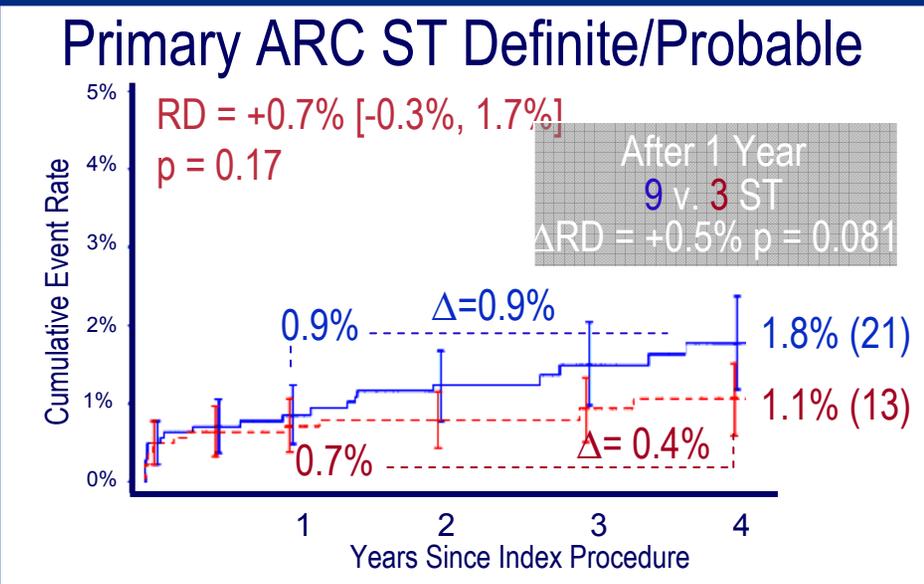
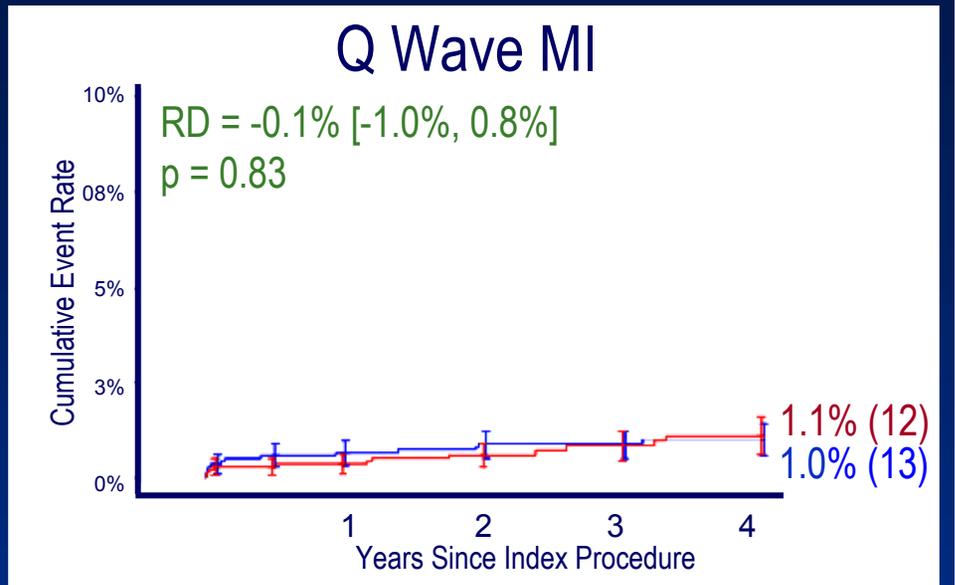
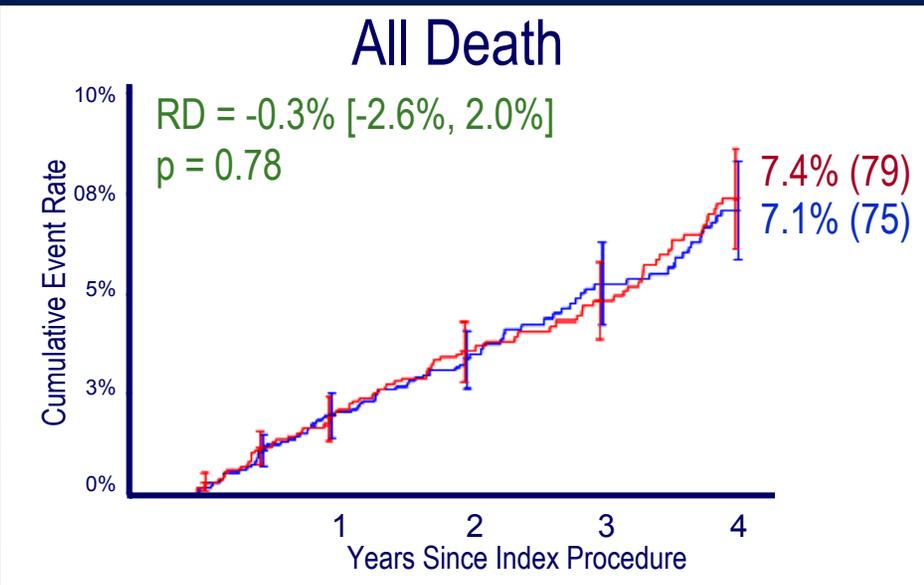
TVR-CABG



Overall TAXUS[®] Stent Analysis (N = 2,797)

Major Events Overview

— TAXUS (N=1400) — BMS (N=1397)
 RD = Rate Difference = TAXUS — BMS
No increase Increase



Overall TAXUS[®] Stent Analysis (N = 2,797)

ANNUAL HAZARD RATES

Δ = Rate Difference = TAXUS — BMS
 No increase (green)
 Increase (red)

Event	0-1 Year (% / patient-year)			
	Taxus	BMS	Risk Difference	
			Δ	p
All Death	1.97	1.90	0.08	0.89
Cardiac Death	1.10	1.31	-0.22	0.60
All MI	4.24	4.76	-0.51	0.52
QWMI	0.66	0.37	0.30	0.28
Total ARC ST All	1.39	1.46	-0.07	0.88
Total ARC ST Def/Prob	0.88	0.81	0.07	0.83
TLR	7.37	17.59	-10.21	<0.0001
TVR-CABG	1.69	3.19	-1.50	0.01

1-4 Years* (% / patient-year)			
Taxus	BMS	Risk Difference	
		Δ	p
1.71	1.87	-0.16	0.65
0.57	0.60	-0.03	0.88
1.01	0.71	0.3	0.23
0.18	0.25	-0.07	0.57
0.72	0.78	-0.06	0.79
0.36	0.25	0.11	0.45
1.57	2.34	-0.77	0.04
0.47	1.04	-0.57	0.01

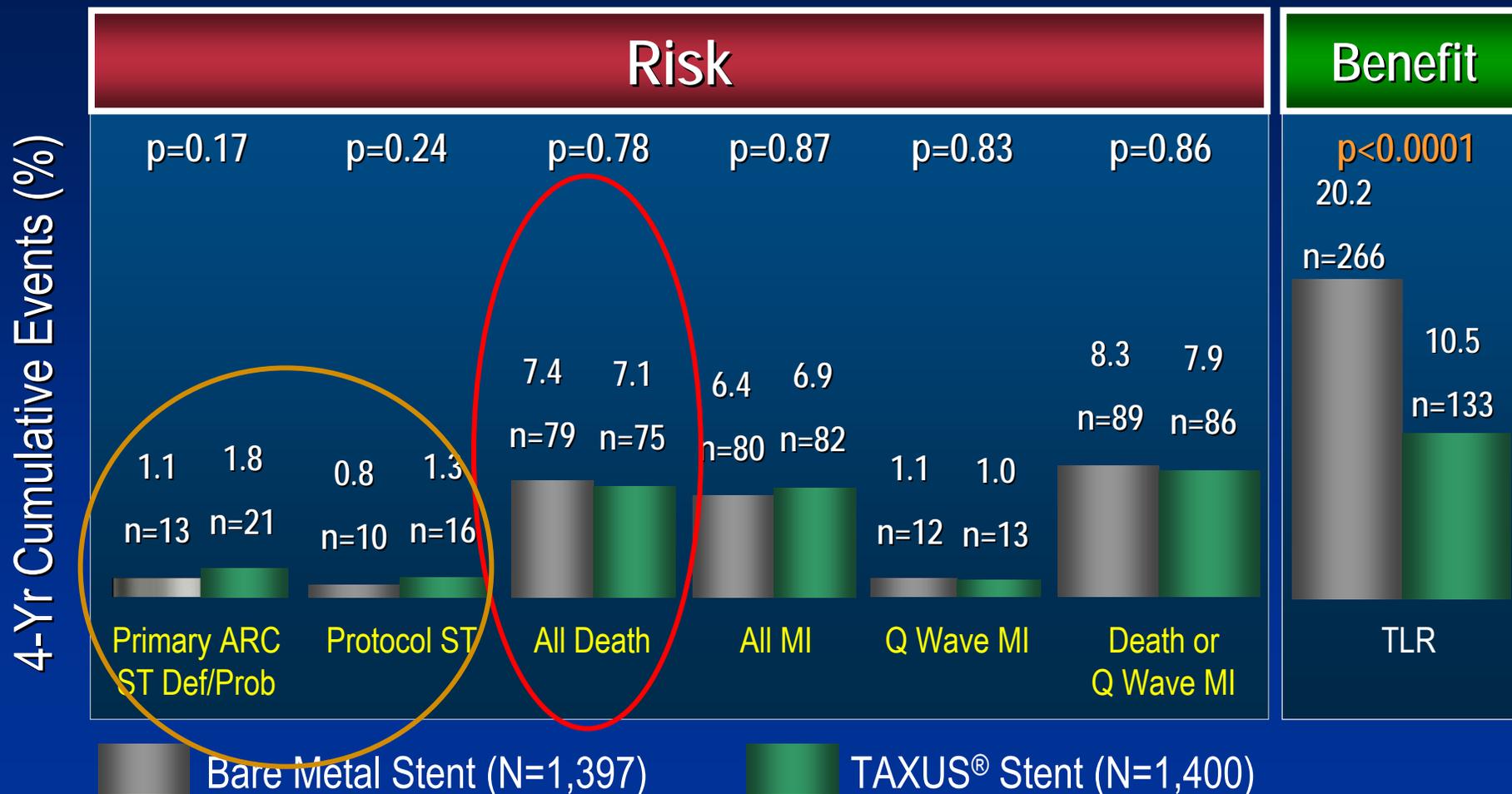
4-year Cumulative Rates (K-M estimate [%])			
Taxus	BMS	Risk Difference	
		Δ	p
7.1	7.4	-0.3	0.78
2.7	3.1	-0.4	0.64
6.9	6.4	0.5	0.87
1.0	1.1	-0.1	0.83
3.5	3.6	-0.1	0.84
1.9	1.5	0.4	0.52
10.5	20.2	-9.7	<0.0001
3.3	6.4	-3.1	0.0004

28 *Includes TAXUS I 4-5 year data.

p-value from Log rank test of no difference in the Kaplan-Meier curves between the groups

TAXUS[®] Stent 4-Year Meta-Analysis reinforces the positive benefit / risk profile

TAXUS I, II-SR, IV, V (N=2,797)

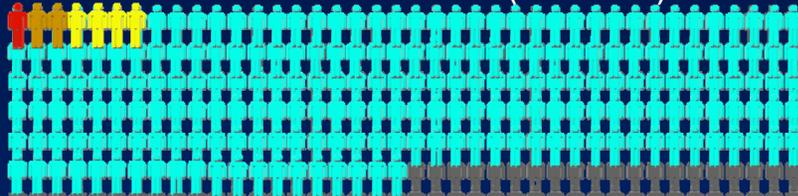


*TAXUS Stent 4-year meta-analysis includes TAXUS I (5 yr), II-SR cohort I (4 yr), IV (4 yr), V (2 yr) (N=2,797). Kaplan Meier estimate and p values from log rank

Restenosis is not benign

Any excess in Death or MI from the 6 additional Protocol-defined stent thromboses with TAXUS is counter-balanced by an offsetting 142-pt reduction in first TLR and TLR-related events

with a bare metal stent (N=1397)



260 TLRs^a 1 Death 2 QMI 5 NQMI

10 STs 3 Deaths 4 QMI 4 NQMI

Stent-Related 4 Deaths 6 QMI 9 NQMI

Other Cardiac 31 Deaths 6 QMI 61 NQMI

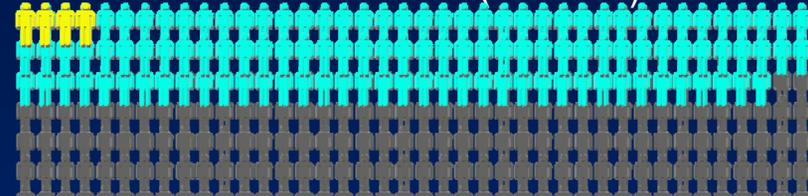
Non-cardiac 44 Deaths

TOTAL 79 Deaths 12 QMI 70 NQMI



= TLR = Death = ST = QMI = Non-QMI

with a TAXUS stent (N=1400)



118 TLRs^b 0 Death 0 QMI 4 NQMI

16 STs 3 Deaths 7 QMI 7 NQMI

Stent-Related 3 Deaths 7 QMI 11 NQMI

Other Cardiac 28 Deaths 6 QMI 60 NQMI

Non-cardiac 44 Deaths

TOTAL 75 Deaths 13 QMI 71 NQMI



a.Exclude 6 TLR due to ST

b.Exclude 13 TLR due to ST; and 2 TLR ≤ 30days.

Agenda

Background

Stent Thrombosis – ARC Definitions

TAXUS Meta-Analysis – All Patients

TAXUS Meta-Analysis – Subgroups

- *Patient groups that traditionally have higher event rates*
 - *Diabetics*
 - *Small vessels (≤ 2.5 mm)*
 - *Long lesions (≥ 28 mm)*
 - *Multiple stents in single vessels*

Antiplatelet Therapy Usage

Summary and Conclusions

TAXUS[®] Stent Subgroup Analysis

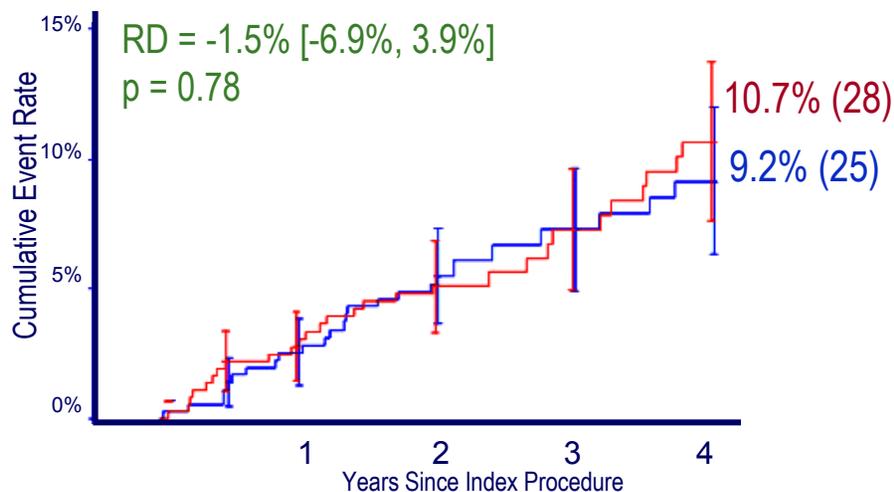
Diabetics (N = 715)

— TAXUS (N=356) — BMS (N=359)

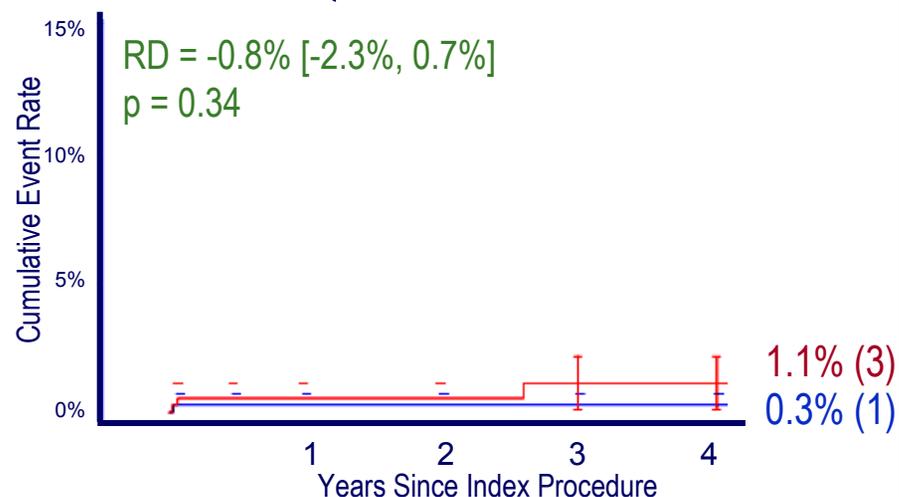
RD = Rate Difference = TAXUS — BMS

No increase Increase

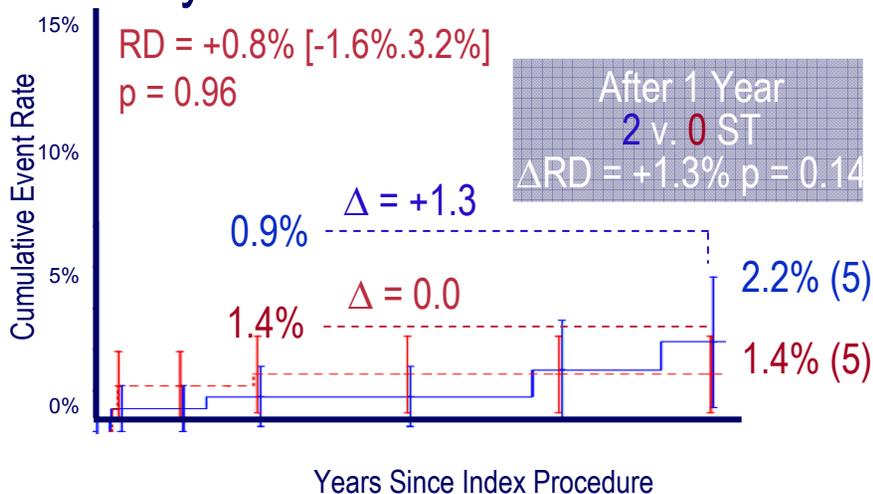
All Death



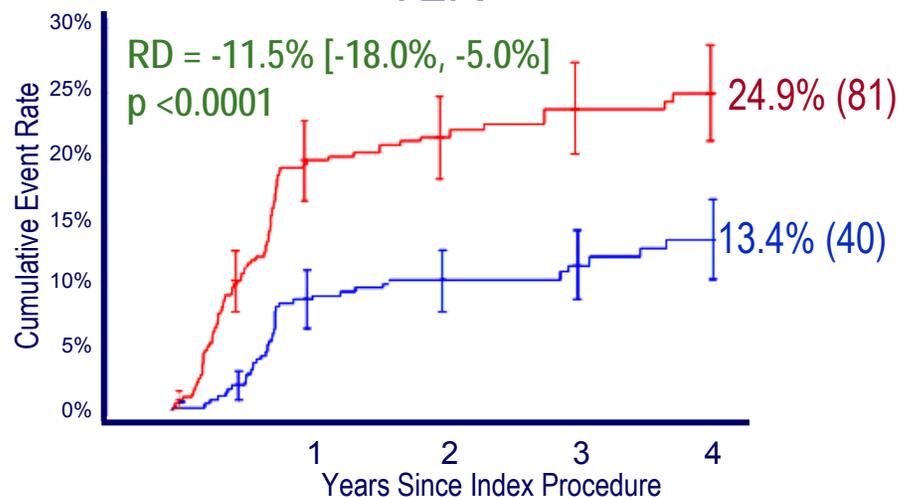
Q Wave MI



Primary ARC ST Definite/Probable



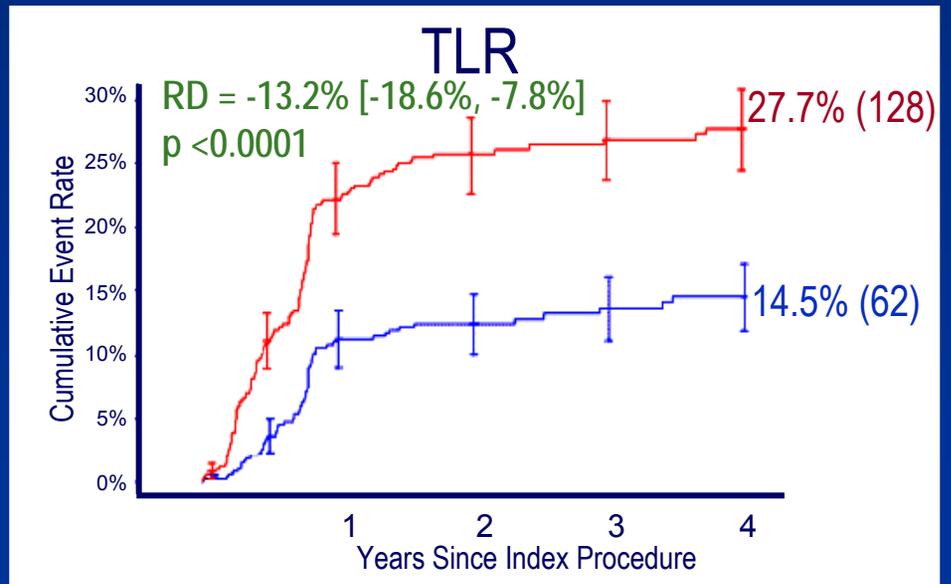
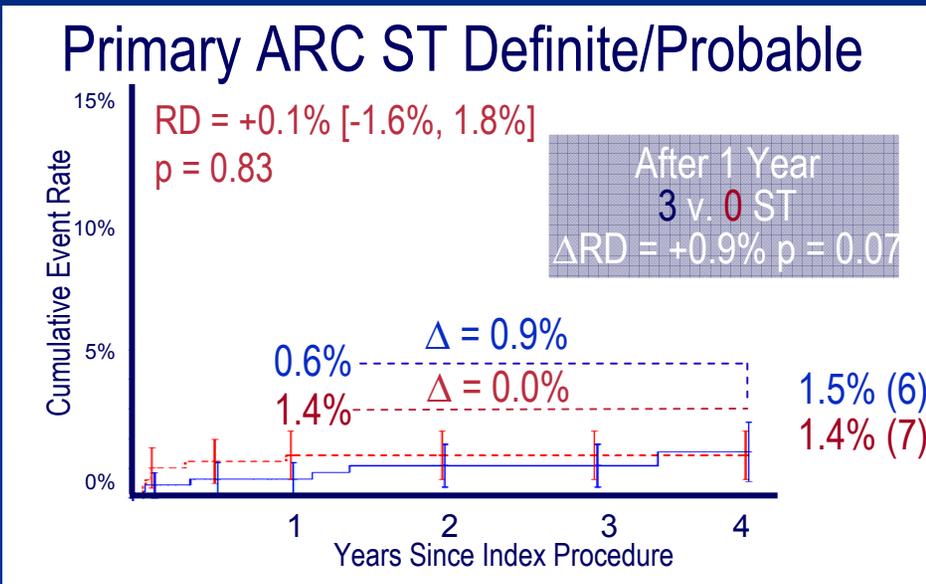
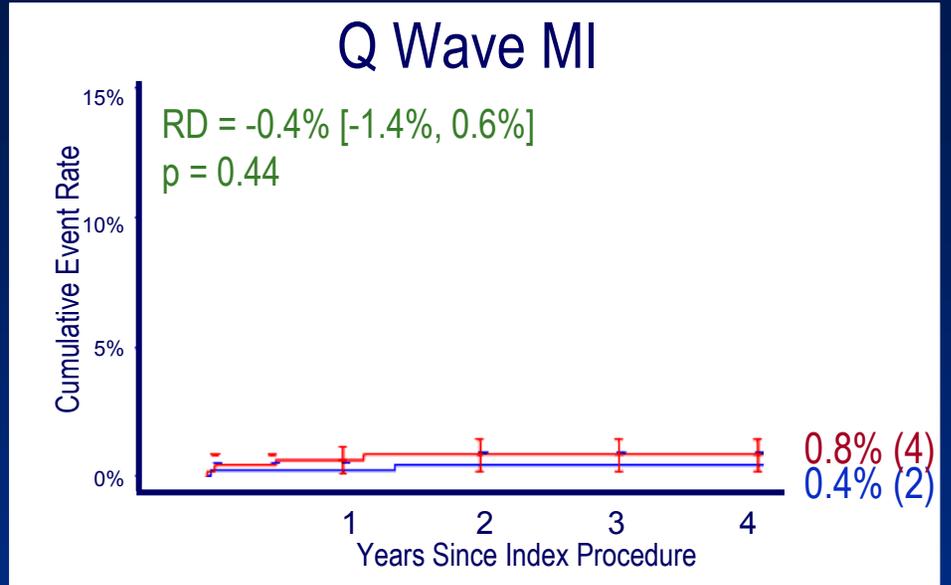
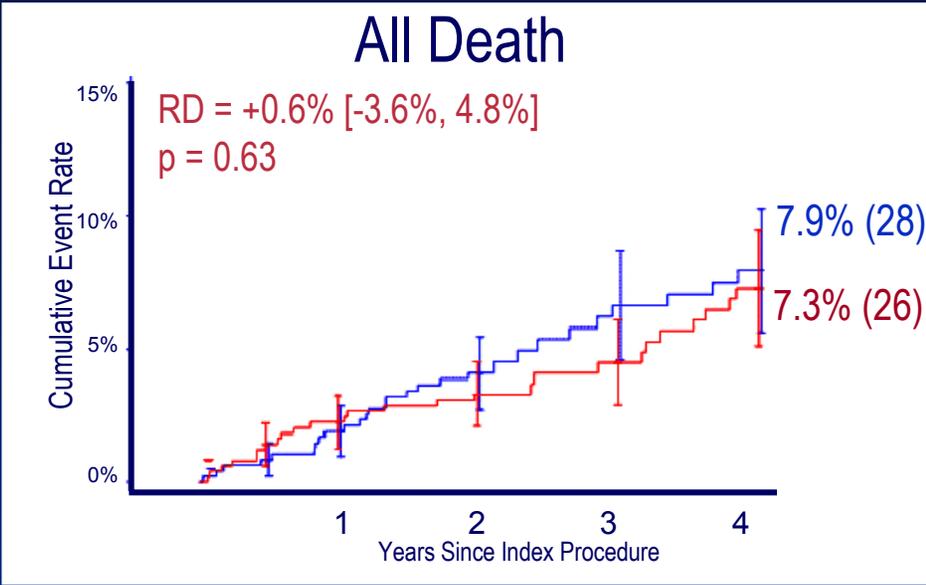
TLR



TAXUS[®] Stent Subgroup Analysis

Small Vessels RVD ≤ 2.5 mm Visual (N = 965)

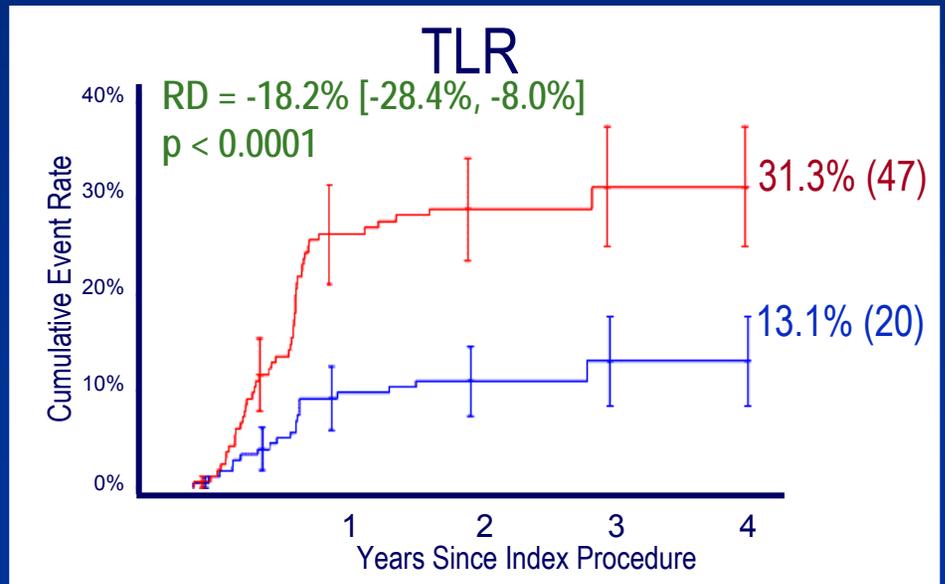
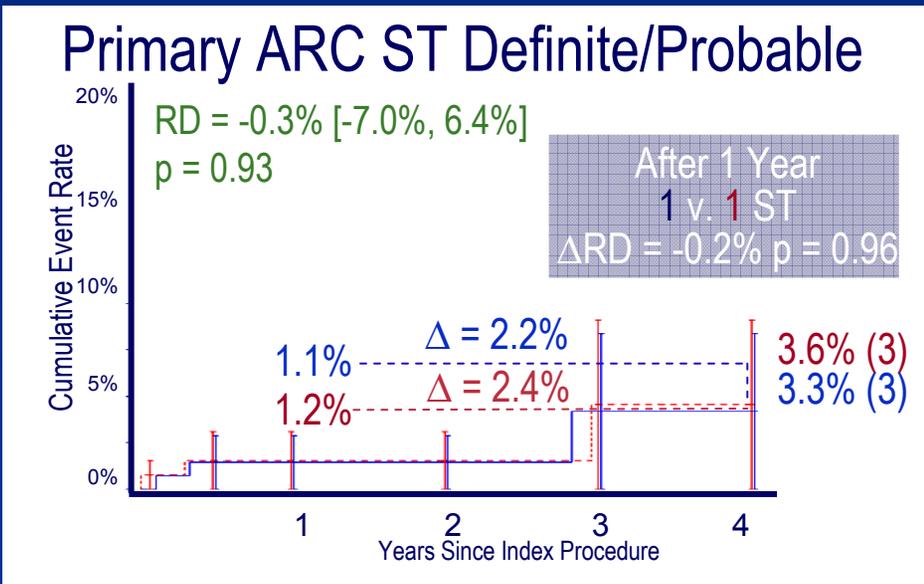
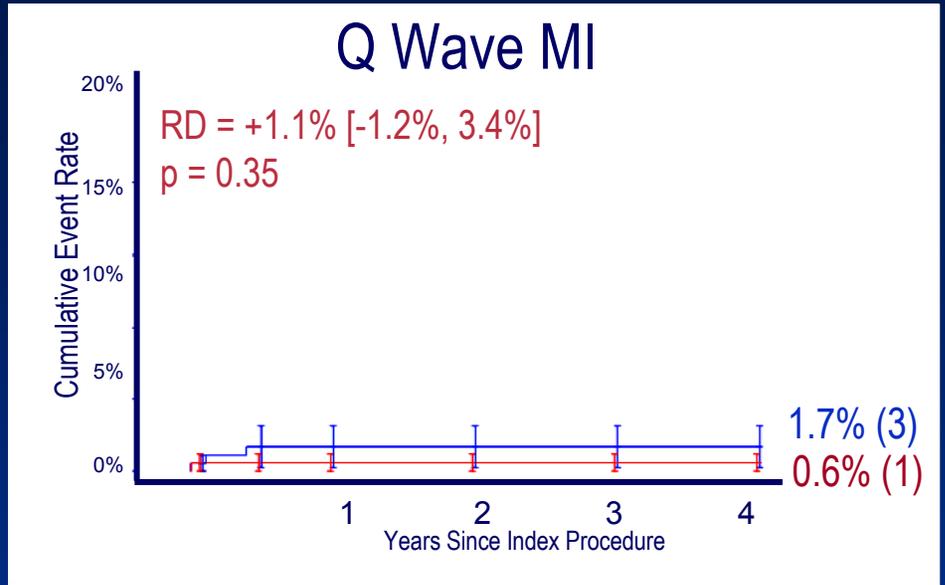
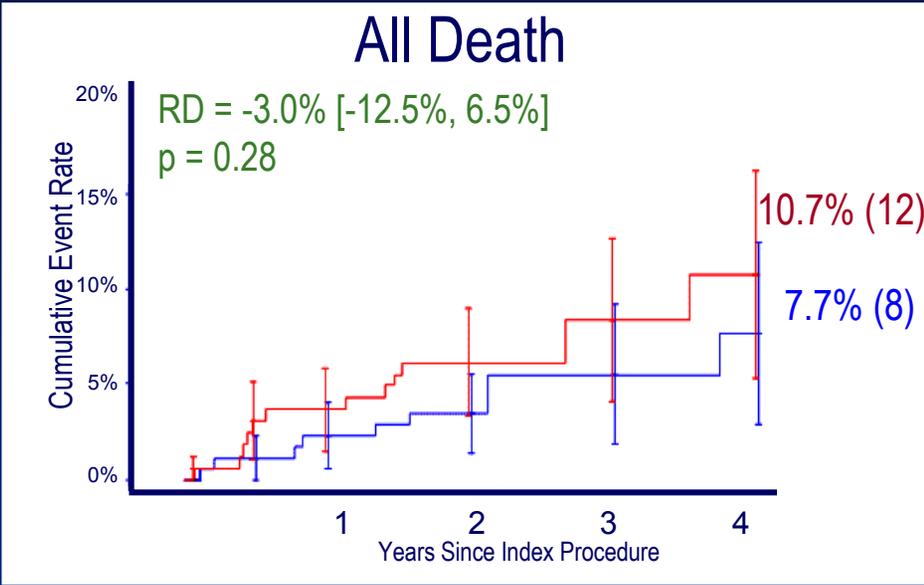
— TAXUS (N=475) — BMS (N=490)
 RD = Rate Difference = TAXUS — BMS
 No increase Increase



TAXUS[®] Stent Subgroup Analysis

Long Lesions $\geq 28\text{mm}$ Visual (N = 341)

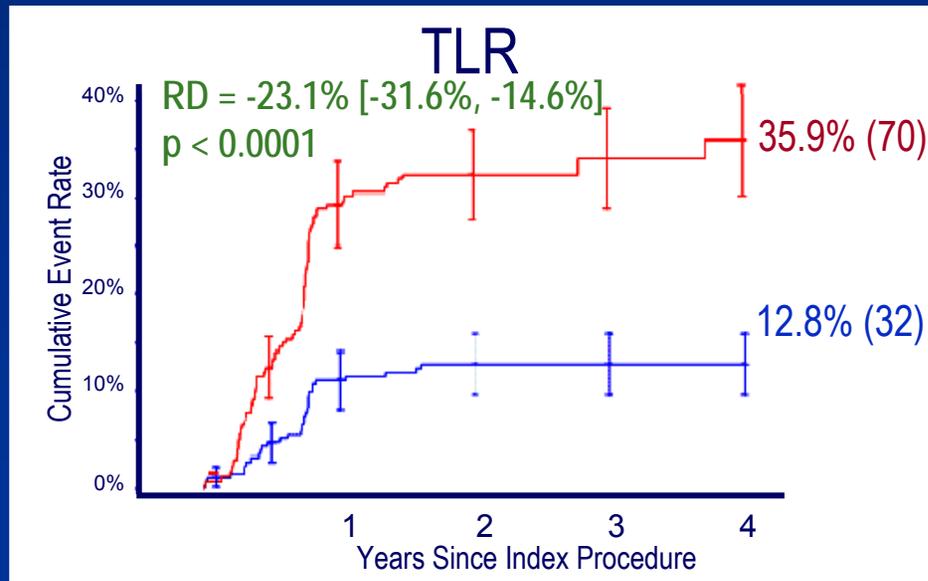
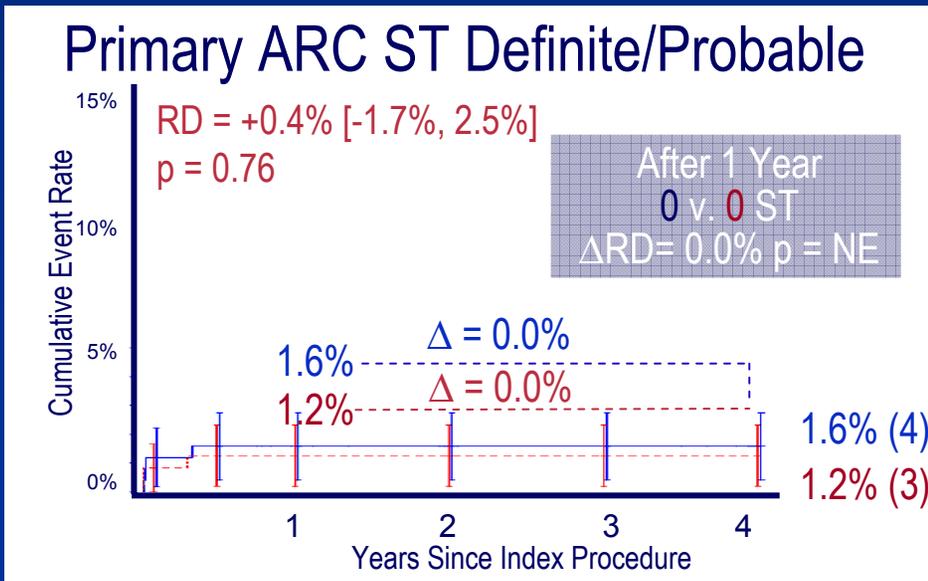
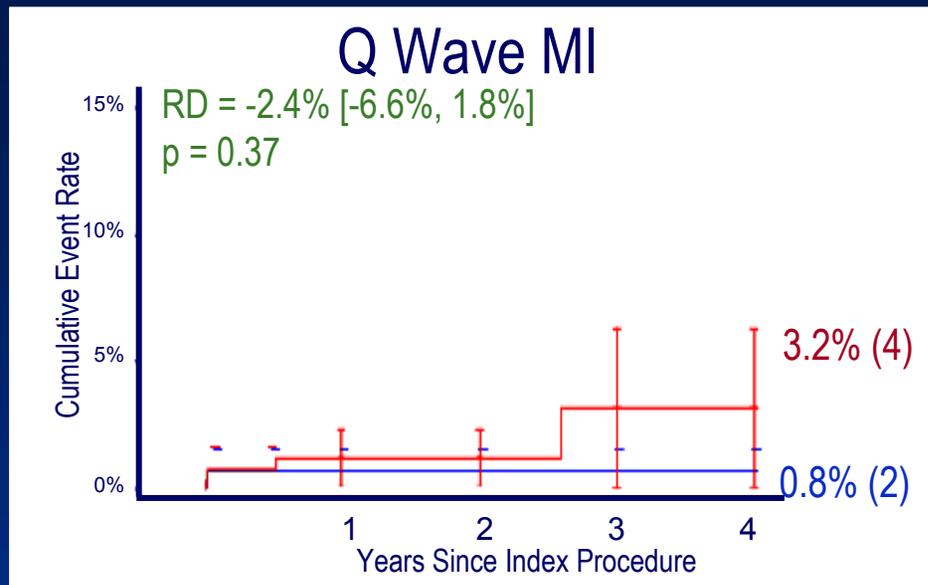
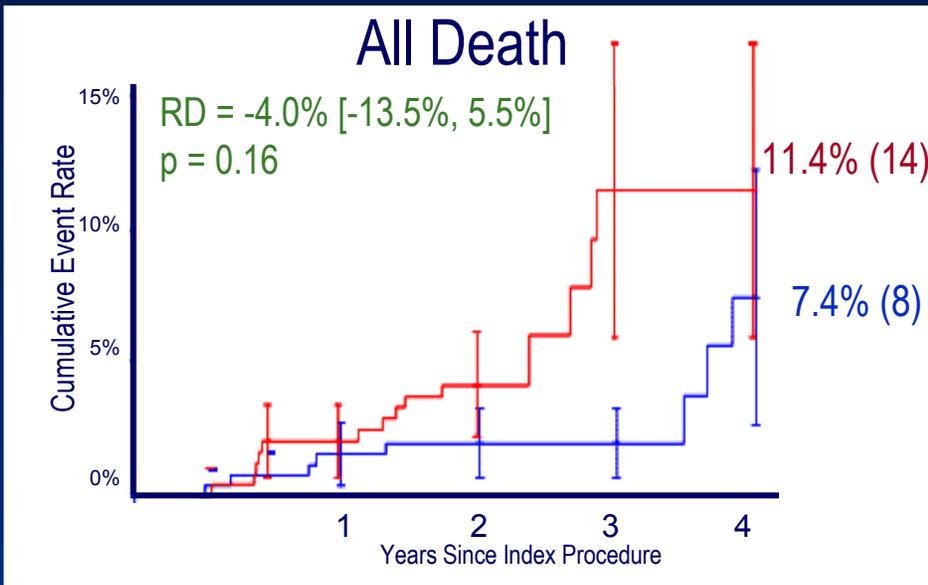
— TAXUS (N=178) — BMS (N=163)
 RD = Rate Difference = TAXUS — BMS
 No increase Increase



TAXUS[®] Stent Subgroup Analysis

Multiple Stents in Single Vessels (N = 497)

— TAXUS (N=255) — BMS (N=242)
 RD = Rate Difference = TAXUS — BMS
 No increase Increase



Summary: TAXUS[®] Stent Subgroup Difference Signals

Δ = Rate Difference = Taxus - BMS
 No increase Increase

Event	1 year	4 year cum	4 year cumulative			
	Overall N= 2797	Overall N=2797	Diabetics N=715	RVD ≤ 2.5mm N= 965	Lesion ≥ 28 N =341	Multiple Stents N=497
All Death	0.08 p=0.89	-0.3 p=0.78	-1.5 p=0.78	0.6 p=0.63	-3.0 p=0.28	-4.0 p=0.16
Cardiac Death	-0.22 p=0.60	-0.4 p=0.64	1.0 p=0.64	-0.4 p=0.95	3.0 p=0.44	2.2 p=0.53
All MI	-0.51 p=0.52	0.5 p=0.87	-0.2	-0.6 p=0.28	9.5 p=0.01	-1.9 P=0.53
QWMI	0.30 p=0.28	-0.1 p=0.83	-0.8 p=0.34	-0.4 p=0.44	1.1 p=0.35	-2.4 p=0.37
Total ARC ST All	-0.07 p=0.88	-0.1 p=0.84	1.5 p=0.79	-0.7 p=0.56	1.1 p=0.90	-0.1 p=0.93
Total ARC ST Def/Prob	0.07 p=0.83	0.4 p=0.52	0.8 p=0.96	-0.4 p=0.48	1.1 p=0.91	-0.1 p=0.94
TLR	-10.21 p<0.0001	-9.7 p<0.0001	-11.5 p<0.0001	-13.2 p<0.0001	-18.2 p<0.0001	-23.1 p<0.0001
TVR-CABG	-1.50 p=0.01	-3.1 p=0.0004	-2.6 p=0.13	-5.1 p=0.0006	-6.9 p=0.02	-5.3 P=0.08

Agenda

Background

Stent Thrombosis – ARC Definitions

TAXUS Meta-Analysis – All Patients

TAXUS Meta-Analysis – Subgroups

Antiplatelet Usage

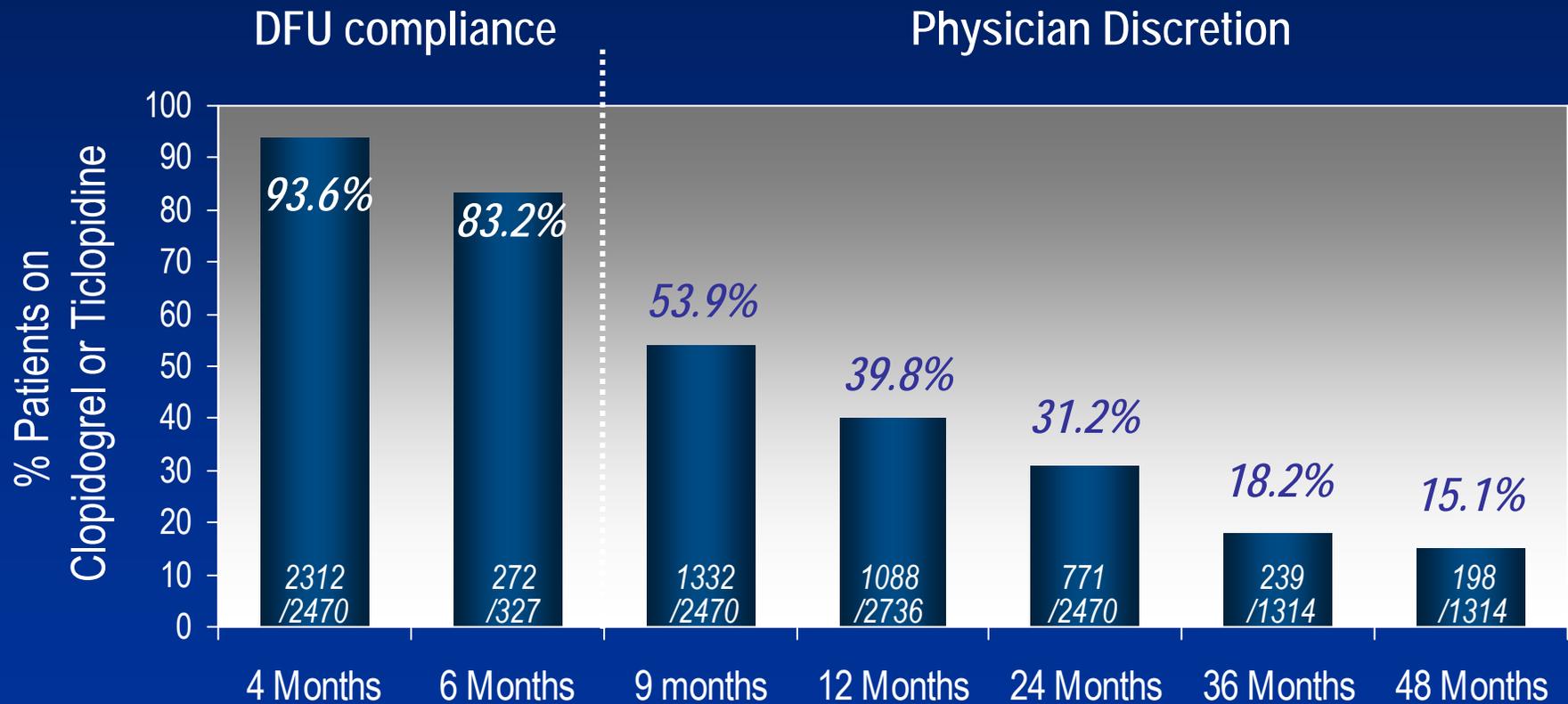
Summary and Conclusions

Long-Term-Thienopyridine Intake in TAXUS Clinical Trial Program

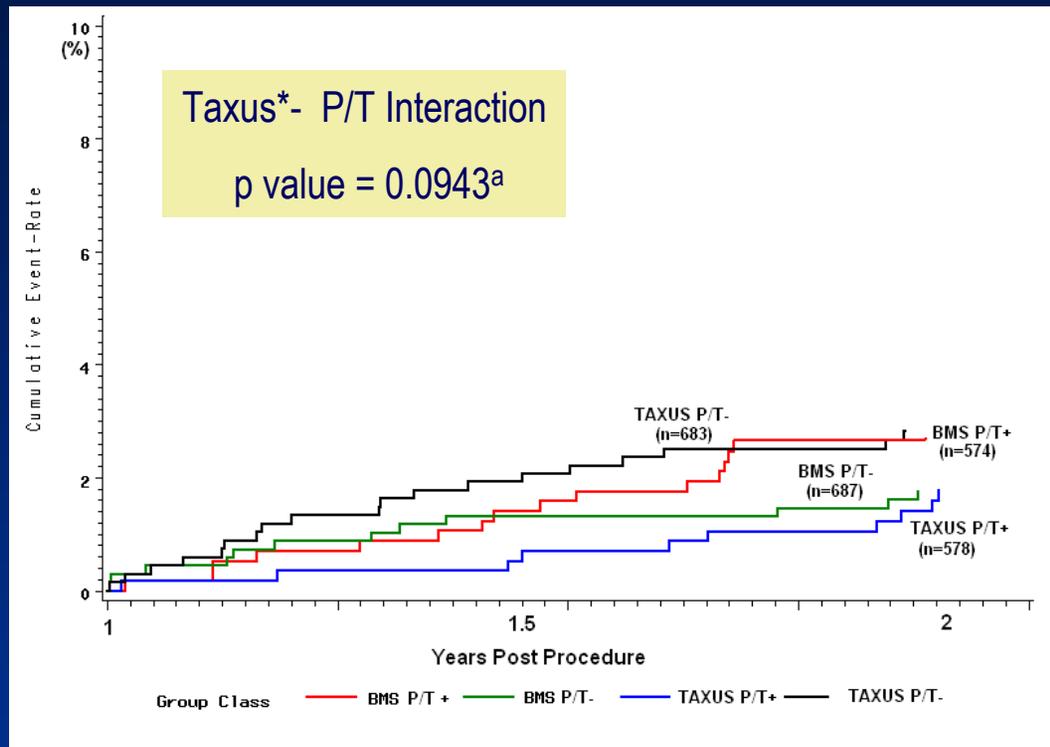
Limitations

No formal medication log

Incomplete data collection between trials at various time points



Death or MI During Follow-up to 2 Years Post-Procedure According to Plavix[®] /Ticlid[®] Usage at 12 Months



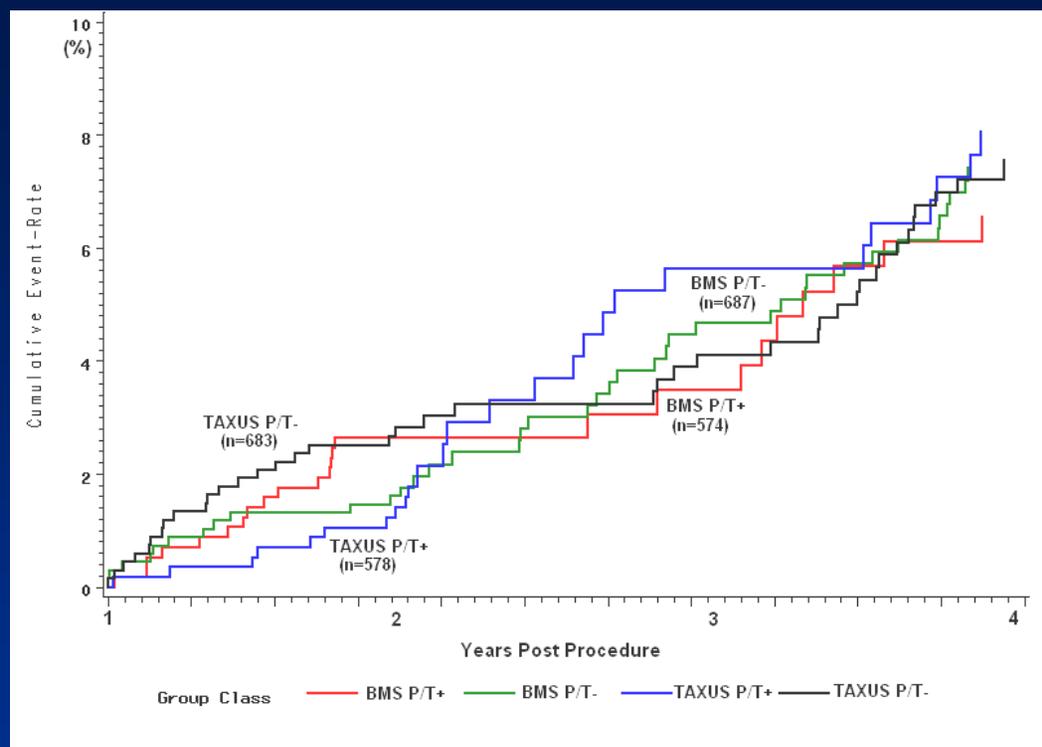
(n=2,522)		Plavix/Ticlid Use Overtime		ASA Use Overtime	
Group	n	12 M Landmark	24 M*	12 M Landmark†	24 M*
BMS P/T+	574	100%	75.9%	97.7%	96.5%
BMS P/T-	687	-	-	97.3%	96.1%
TAXUS P/T+	578	100%	73.7%	96.9%	96.5%
TAXUS P/T-	683	-	-	96.1%	93.2%

† Medication data available in TAXUS 2, 4, and 5 only

* Medication data available in TAXUS 4, 5 only

a. adjusted Cox regression model, additionally adjusted for patient baseline and lesion characteristics
Plavix and Ticlid are trademarks of Sanofi-Aventis

Death or MI During Follow-up to 4 Years Post-Procedure According to Plavix® /Ticlid® Usage at 12 Months



† Medication data available in TAXUS 2, 4, 5

* Medication data available in TAXUS 4, 5, only

** Medication data available in TAXUS 4 only

(n=2,522)		Plavix/Ticlid Use Overtime				ASA Use Overtime			
Group	n	12 M Landmark	24 M*	36 M**	48 M**	12 M Landmark†	24 M*	36 M*	48 M**
BMS P/T+	574	100%	75.9%	70.1%	63.6%	97.7%	96.5%	93.2%	92.7%
BMS P/T-	687	-	-	-	-	97.3%	96.1%	95.0%	91.7%
TAXUS P/T+	578	100%	73.7%	66.2%	60.6%	96.9%	96.5%	92.5%	89.5%
TAXUS P/T-	683	-	-	-	-	96.1%	93.2%	91.3%	90.4%

Summary -- On-label uses of the Taxus[®] SR Stent System

The Taxus I, II, IV, and V randomized trials compared the TAXUS[®] Slow-Release (SR) Stent to Bare Metal Stent (BMS) controls in 2,797 patients, median 4 year follow-up:

- a PROFOUND *clinical benefit* reduction in repeat revasc. ($\Delta - 9.7\%$, or 48 % relative)
- with trends towards LESS Death ($\Delta -0.3\%$) or Q-MI ($\Delta -0.1\%$) through last follow-up

This favorable risk benefit was seen in all studied sub-groups, with TLR reductions of :

- Diabetics (n=715) $\Delta - 11.5\%$, (46% relative), $p < 0.0001$
- Small vessels ($\leq 2.5\text{mm}$) (n=965) $\Delta - 13.2\%$, (48% relative), $p < 0.0001$
- Long Lesions $\geq 28\text{ mm}$ (n=341) $\Delta - 18.2\%$, (58% relative), $p < 0.0001$
- Multiple Stents/vessel (n=497) $\Delta - 23.1\%$, (64% relative), $p < 0.0001$

Stent thrombosis rates were not statistically different from the BMS Control for either :

	<u>4 years cum.</u>	or	<u>beyond 1 year (VLST)</u>
per protocol	1.3 vs. 0.8 %		$\Delta +0.4\%$, $p = 0.057$
ARC 1 ^o def.+prob.	1.8 vs. 1.1 %		$\Delta +0.5\%$, $p = 0.081$
ARC Total	3.5 vs. 3.6 %		$\Delta - 0.1\%$, $p = 0.786$

Plavix use beyond 6 months with TAXUS showed a trend towards reduced Death or MI

Thank you

DISCUSSION SLIDES

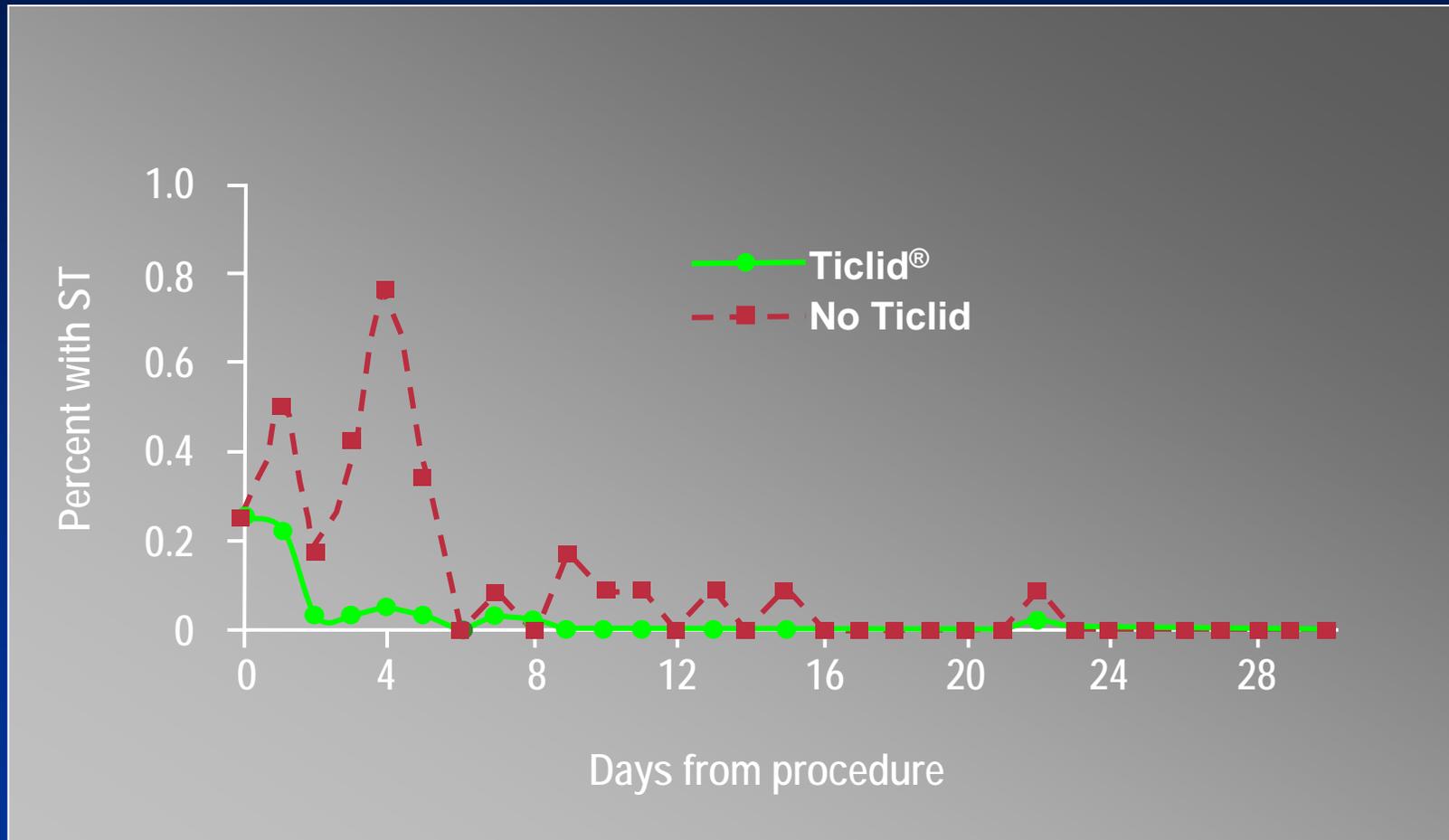
Background

- Drug-eluting stents are a major new breakthrough for reducing restenosis and the need for re-intervention in PCI procedures
- The potent anti-proliferative drugs and the polymers that release them clearly and significantly alter vascular biological reaction, with the benefit of reduced in-stent restenosis and repeat revascularization
- They may, however, also cause *unintended consequences* such as delayed or incomplete endothelial coverage, inflammation, or positive remodeling, each of which have now been observed in man
- There have been suggestions that these consequences may lead to increases in adverse events (stent thrombosis after 1 year, late MI, or late death) compared to traditional bare metal stents
- If there were net increases in late death or MI with DES versus BMS, they might offset the potential benefits of reduced restenosis, and potentially lead to restrictions on DES use

Background

Time course of Stent Thrombosis with BMS

Rationale for 1 month Duration of Anti-platelet Therapy



2-4 weeks duration of anti-platelet therapy adequate for BMS

BMS = bare metal sent; ST = stent thrombosis.
Cutlip DE et al. *Circulation*. 2001;103:1967.

Number of Stent Thrombosis Cases

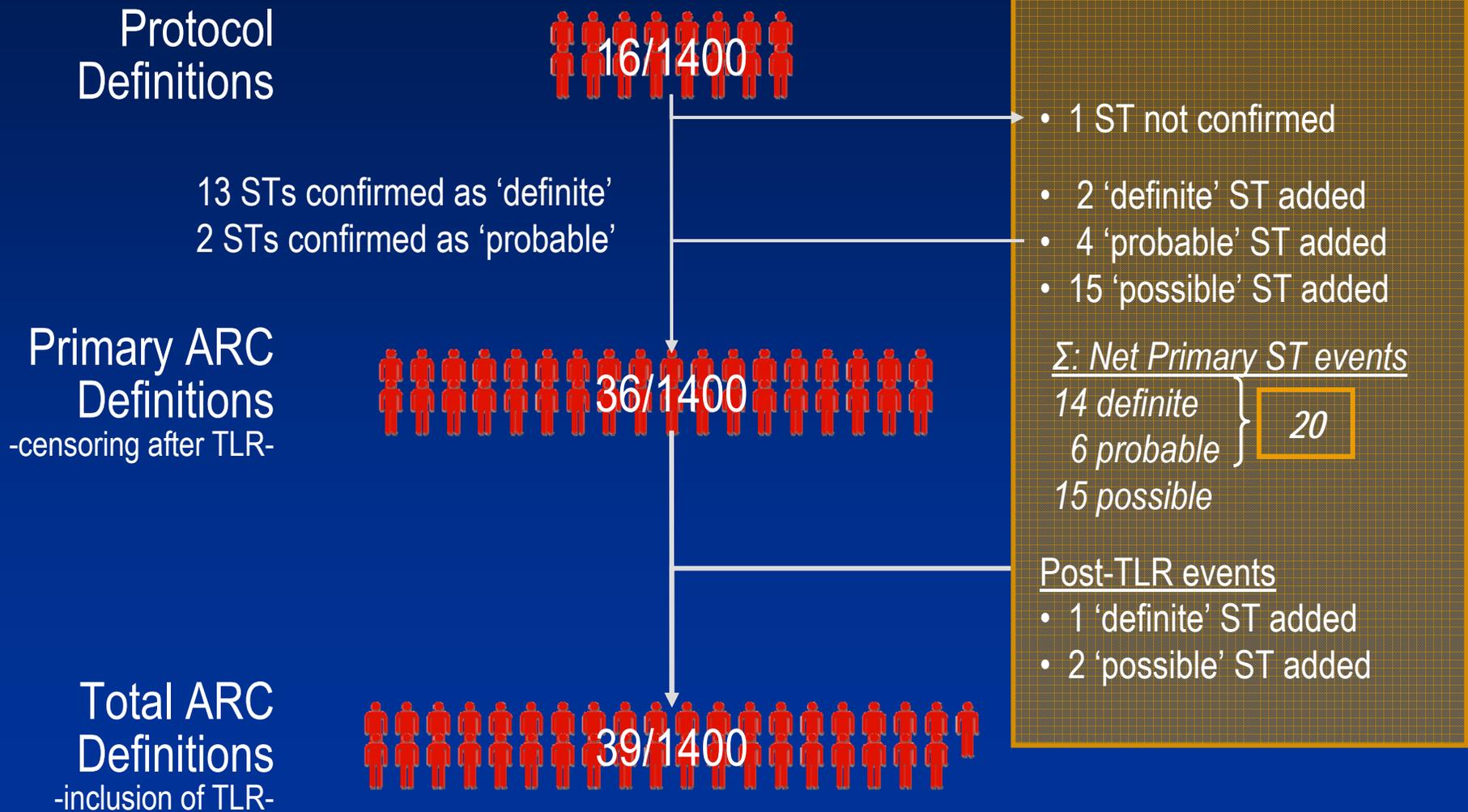
BSC vs. ARC Definitions

ALL Stent Thrombosis Grouped by Days from Index Procedure

		Days from Index Procedure				TOTAL
		0 - 1	2-30	31-365	366+	
BSC Protocol	TAXUS	3	4	3	6	16 ^a
	Control	3	6	2	1	10 ^a
All ARC Definitions (Primary = Not post-TLR)	TAXUS	3	4	3 + 8	6 + 12 = 18	36 ^a
	Control	3	6	2 + 9	1 + 15 = 16	33 ^a
All ARC Definitions (Total = with post-TLR)	TAXUS	3	4	3 + 9	6 + 14 = 20	39 ^a
	Control	3	6	2 + 11	1 + 21 = 22	41 ^a

a. Patients may have multiple ST in different categories.

Patient flow in TAXUS Group – Impact of ARC reassessment



Patient flow in Control Group – Impact of ARC reassessment

ARC Reassessment

- 2 'definite' ST added
- 2 'probable' ST added
- 20 'possible' ST added *

Σ : Net Primary ST events

10 definite
3 probable
20 possible

13

Post-TLR events

- 4 'definite' ST added
- 1 'probable' ST added
- 3 'possible' ST added

10/1397

Protocol
Definitions

8 STs confirmed as 'definite'
1 ST confirmed as 'probable'
1 ST confirmed as 'possible'

33/1397

Primary ARC
Definitions
-censoring after TLR-

41/1397

Total ARC
Definitions
-inclusion of TLR-

- One patient had a probable and possible event

Details about ST after TLR in TAXUS



Case 1

Definite ST on day 924 – after 3 (!!) TLRs attempts with cutting balloon and brachytherapy each on days 517, 593, and 924



Case 2

Possible ST on day 185 - 70 days after TLR with a BMS plus brachytherapy



Case 3

Possible ST on day 439 – 229 days after TLR with two BMS

Details about ST after TLR in Control -1-



Case 1

Definite ST on day 329 – 137 days after TLR with cutting balloon and brachytherapy (subsequent 90% restenosis)



Case 2

Two (!!) definite STs on days 429 and 569 – after 3 revascularizations (day 85 with cutting balloon and brachytherapy, day 283 with 2 TAXUS stents (no restenosis), and day 429 with CYPHER (!!) in neighboring side branch)



Case 3

Three (!!) definite STs on days 607, 611, and 640 – after 4 revascularizations (day 293 with cutting balloon and brachytherapy, day 607 with TAXUS outside of target vessel, day 610 with TAXUS in target lesion, and day 640 (failed attempt) with medical therapy)



Case 4

Definite ST on day 941 – 669 days after TLR with cutting balloon and brachytherapy

Details about ST after TLR in Control -2-



Case 5

Probable ST on day 553 – 245 days after TLR with stent



Case 6

Possible STs on day 143 – 3 days after TLR with atherectomy and brachytherapy



Case 7

Possible ST on day 620 – 258 days after TLR with brachytherapy

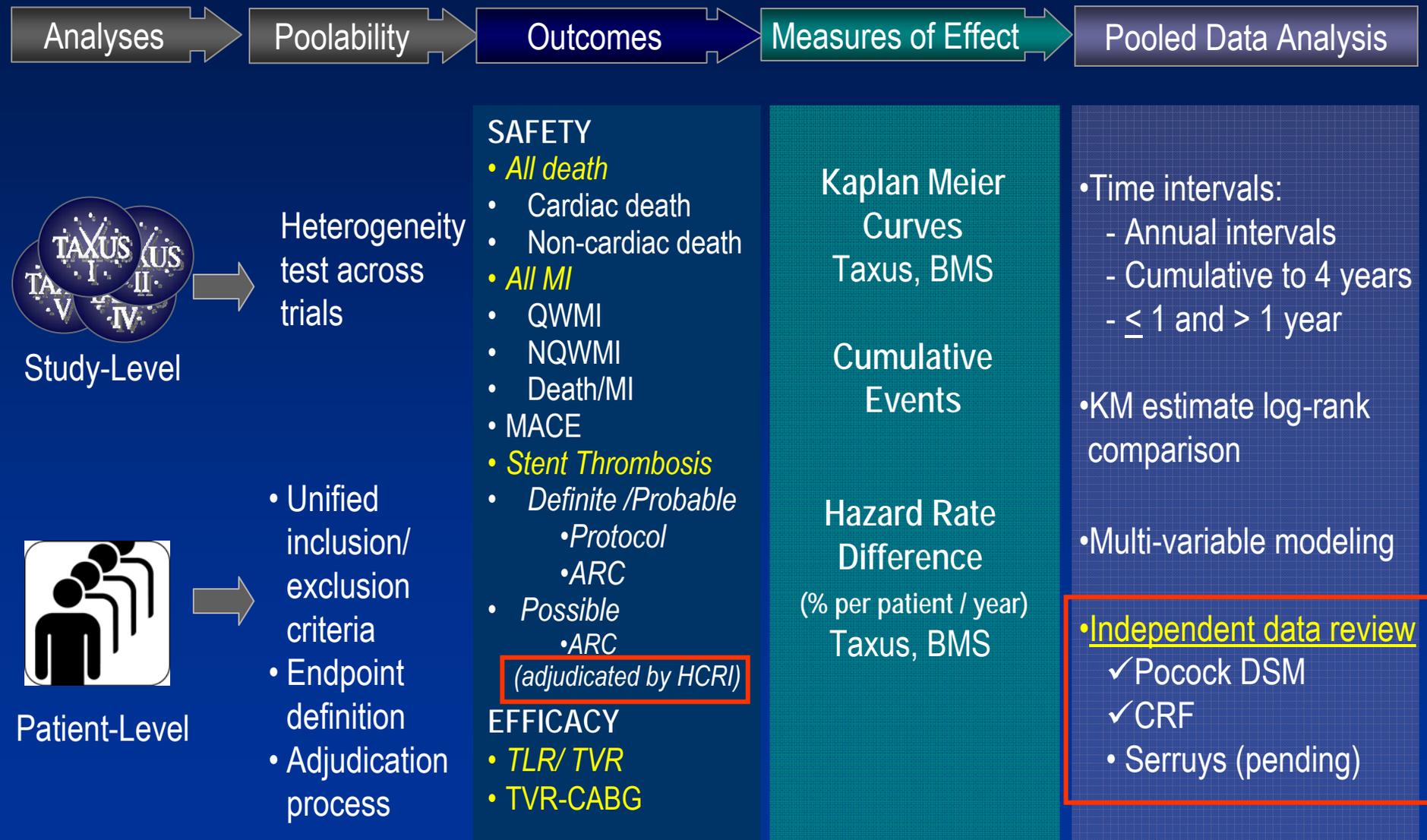


Case 8

Possible ST on day 1125 – 846 days after cutting balloon and brachytherapy

Methodology and Data Synthesis

Outside adjudication of all endpoints; independent review of all data



Cypher[®] Prior TLR and Stent Thrombosis

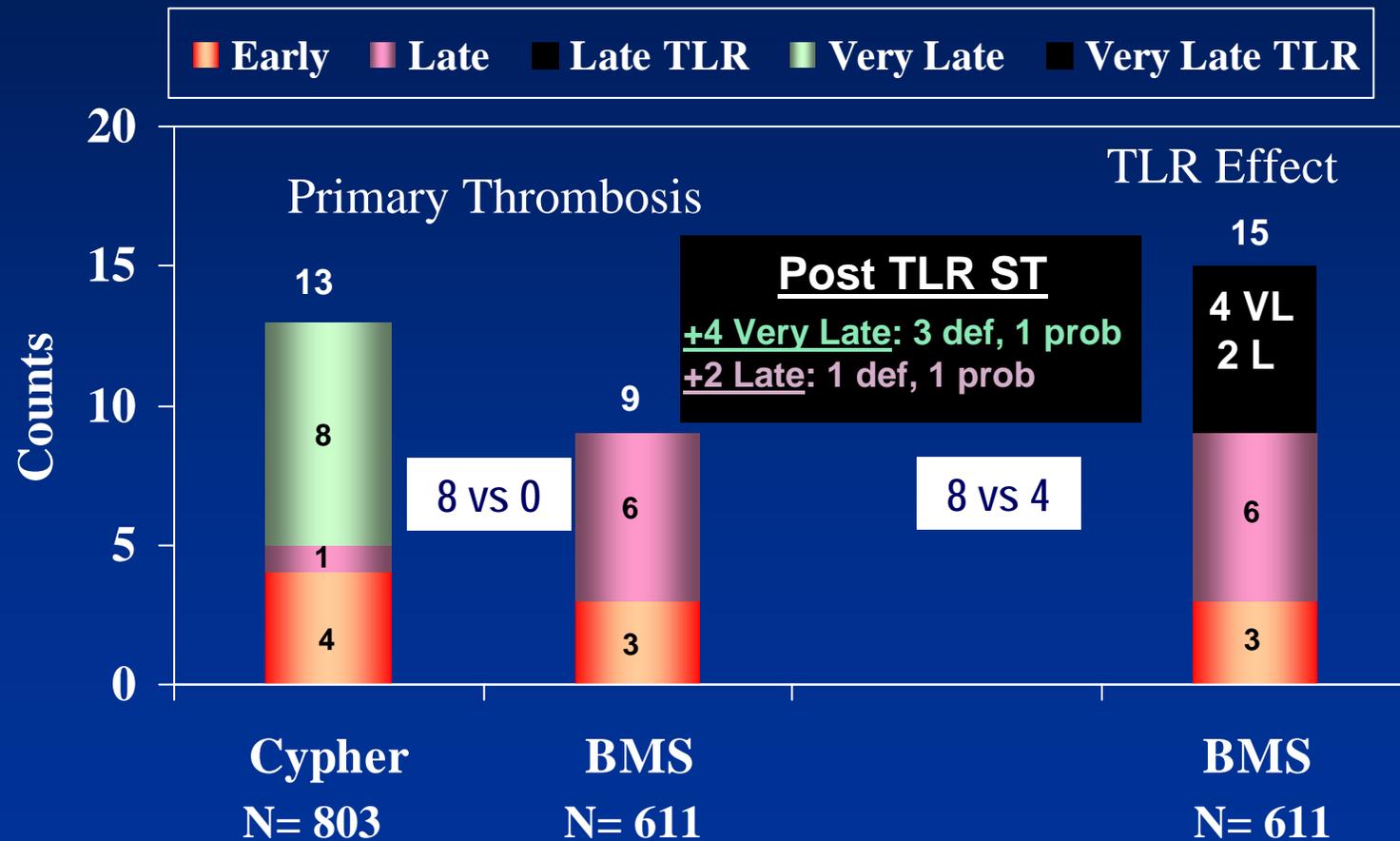
Don Cutlip, presentation at TCT 2006

	DES ST (any) N = 27	BMS ST (any) N = 27
Prior TLR	<p>QUESTION: Does a late thrombosis following brachytherapy to treat a BMS in-stent restenosis REALLY count <i>mechanistically</i> as a BMS stent thrombosis?</p> <p>Or is it preferable to still censor such events from our <i>mechanistic</i> understanding of whether DES thrombose more than BMS, knowing that we can capture any missed events in our intent to treat analysis of Death and MI?</p>	
Time from		
ST Classifi		
TLR Procedure	0	10 (7/10 brachy)
BMS only	0	0
Any SES	0	1
PTCA only	0	2
Brachytherapy/PTCA	0	5
Brachytherapy/stent	0	2

* 1 Patient had stent thrombosis 1539 days after procedure.

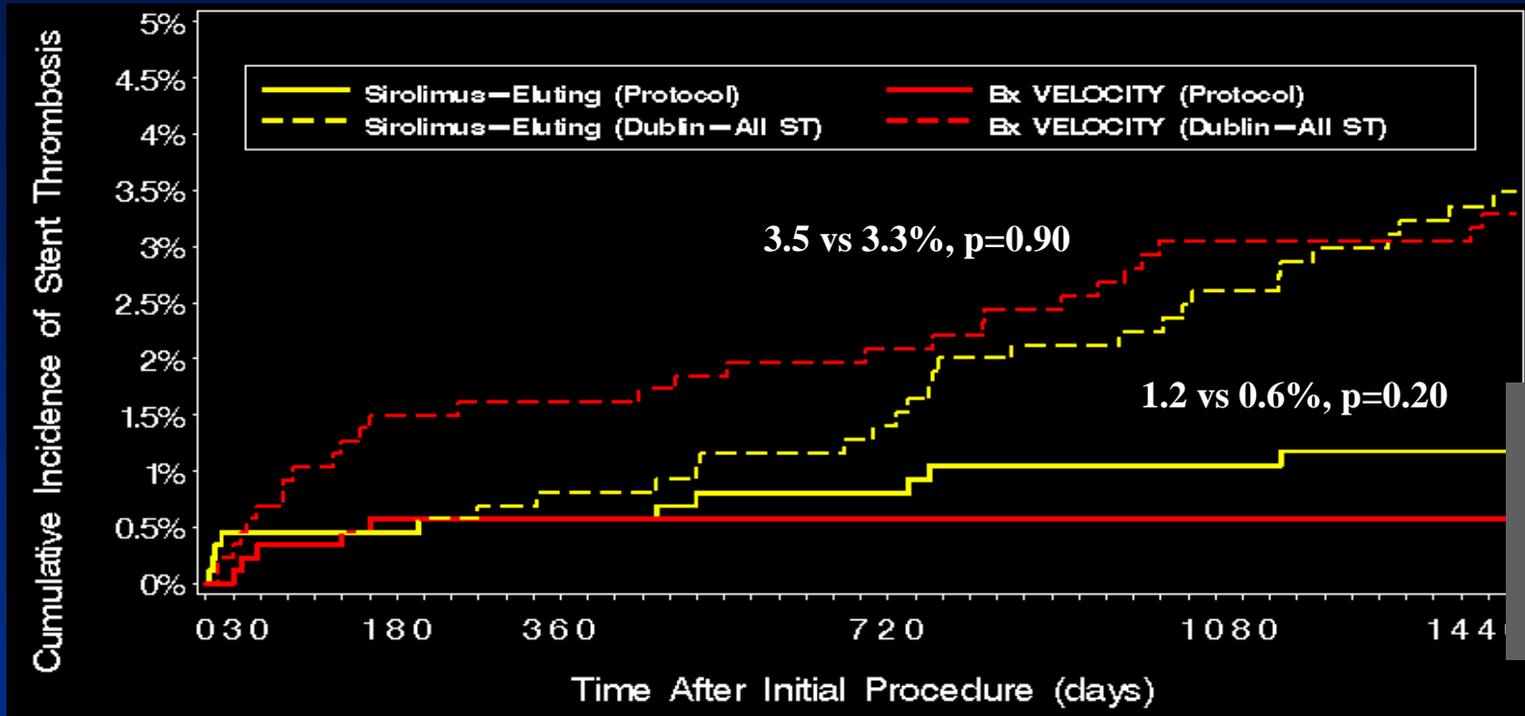
Cypher® Primary Stent Thrombosis

Counts of Definite/Probable Thrombosis – Prior TLR Effect



Modified minimally from Don Cutlip, presentation at TCT 2006

The difference is profound!



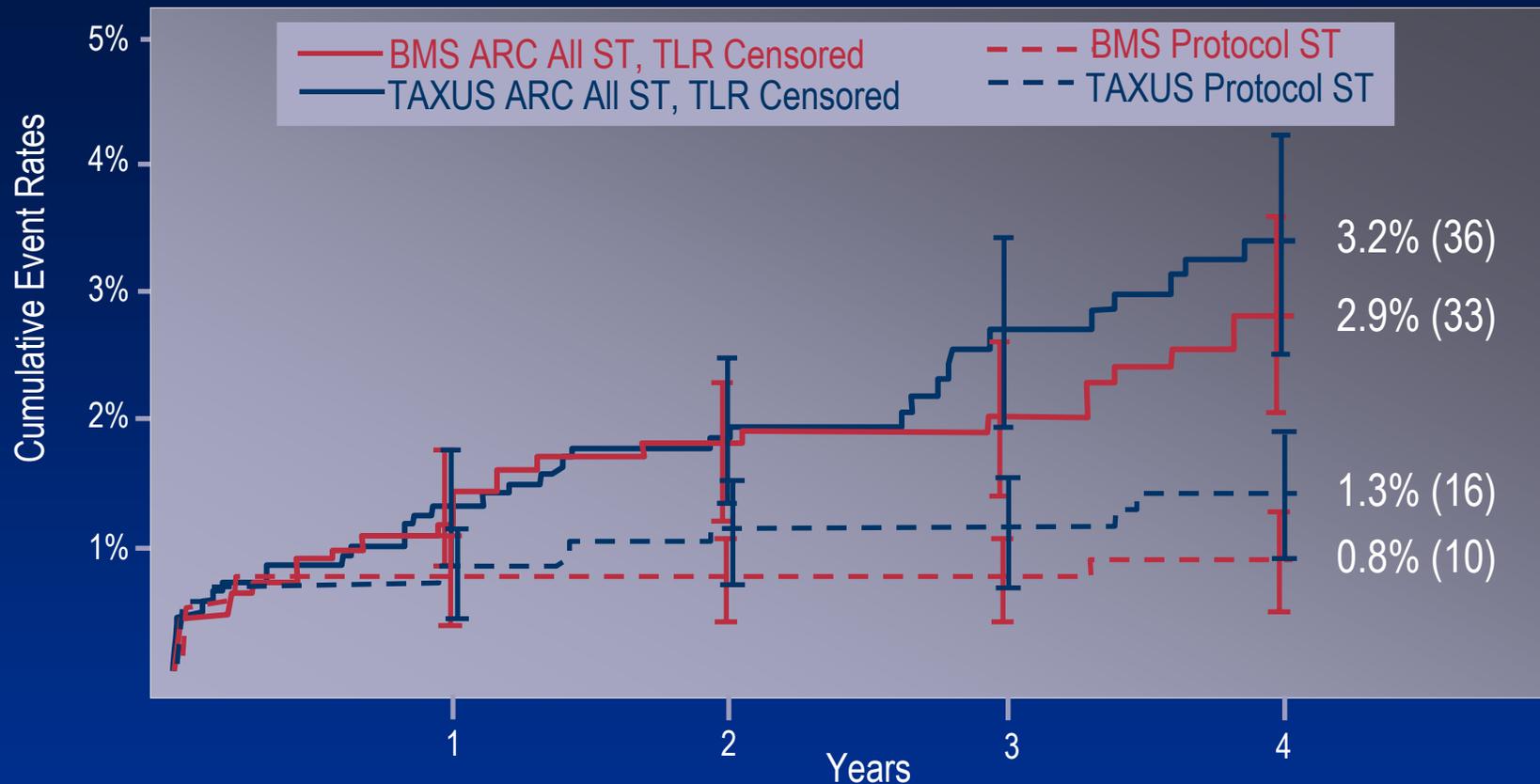
Cypher

BMS

Days	30	90	360	720	1080	1440
# Entered	878	872	860	831	806	801
# Events	4	0	2	5	10	8
# Entered	870	867	853	830	809	805
# Events	3	5	6	4	9	1

Cutlip TCT 2006

Taxus the difference is profound!

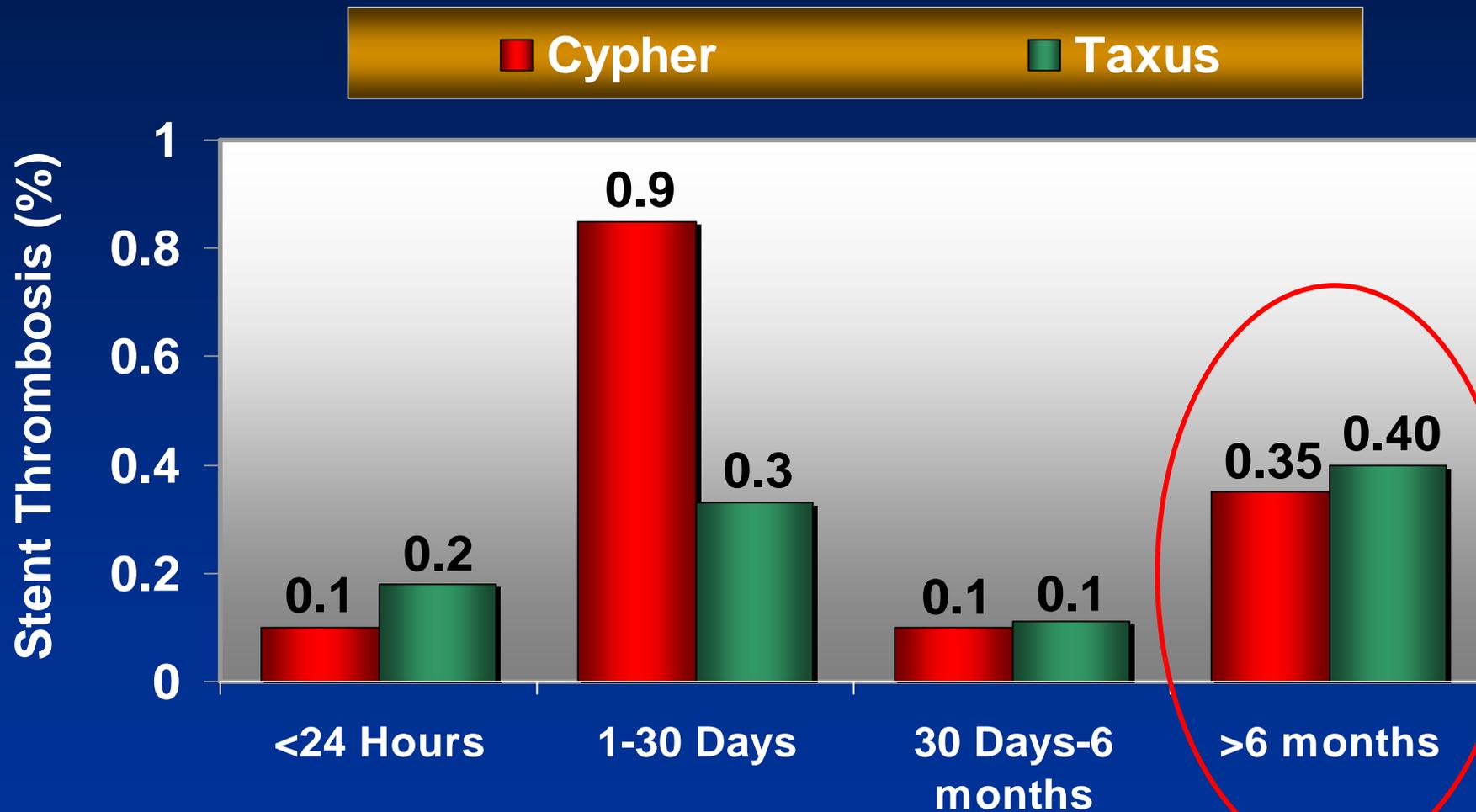


	Years	1		2		3		4	
		ARC	Protocol	ARC	Protocol	ARC	Protocol	ARC	Protocol
TAXUS	# Entered	1400	1400	1359	1361	1336	1338	1216	1217
	# Events	18	10	8	4	6	0	4	2
BMS	# Entered	1397	1397	1362	1363	1335	1342	1231	1238
	# Events	18	9	6	0	2	0	7	1

Background

Parity confirmed in broader data sets

ESTROFA : Stent thrombosis incidence



Dr. de la Torre, TCT 2006

(13,500 DES @15 Spanish Centers)

TAXUS Diabetics (N = 715)

Annual Event Rates

Δ = Rate Difference = TAXUS — BMS
 No increase (green)
 Increase (red)

Event	0-1 Year (% / patient-year)			
	Taxus	BMS	Rate Difference	
			Δ	p
All Death	2.60	2.84	-0.25	0.84
Cardiac Death	1.73	1.99	-0.26	0.80
All MI	3.57	6.28	-2.72	0.12
QWMI	0.29	0.57	-0.28	0.57
ST Protocol	0.58	1.43	-0.86	0.27
Total ARC ST All	1.74	2.29	-0.56	0.61
TLR	8.95	21.81	-12.86	<0.0001
TVR-CABG	2.62	4.67	-2.05	0.16

1-4 Years (% / patient-year)			
Taxus	BMS	Rate Difference	
		Δ	p
2.52	2.70	-0.18	0.85
1.11	0.60	0.50	0.33
1.28	0.61	0.68	0.21
0.00	0.15	-0.15	0.34
0.16	0.00	0.16	0.30
0.95	0.60	0.35	0.48
2.09	2.46	-0.37	0.66
0.95	1.37	-0.41	0.53

4-year Cumulative Rates (K-M estimate [%])			
Taxus	BMS	Rate Difference	
		Δ	p
9.2	10.7	-1.5	0.78
4.4	3.4	1.0	0.64
7.2	7.4	-0.2	0.57
0.3	1.1	-0.8	0.34
1.2	1.4	-0.2	0.50
4.6	3.1	1.5	0.79
13.4	24.9	-11.5	<0.0001
7.2	9.8	-2.6	0.13

p-value from Log rank test of no difference in the Kaplan-Meier curves between groups

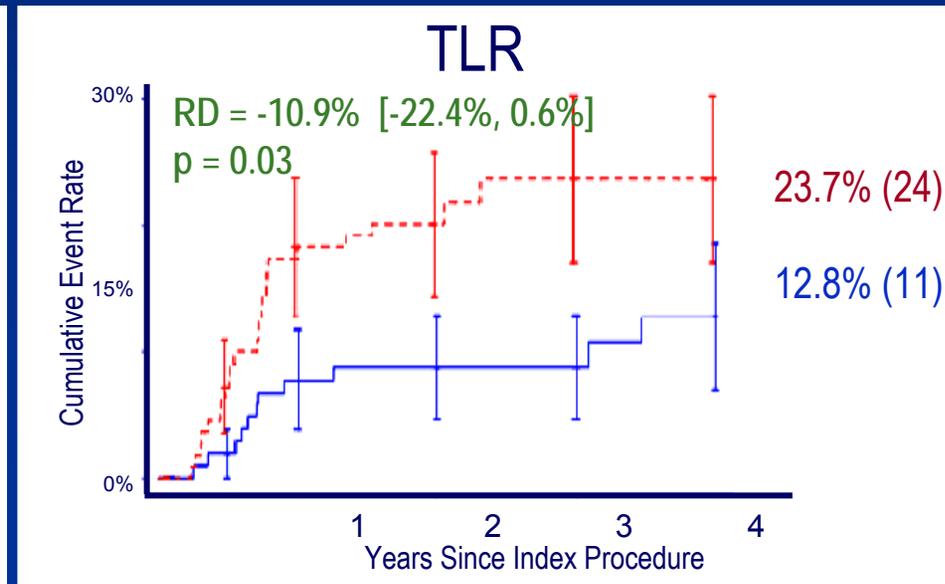
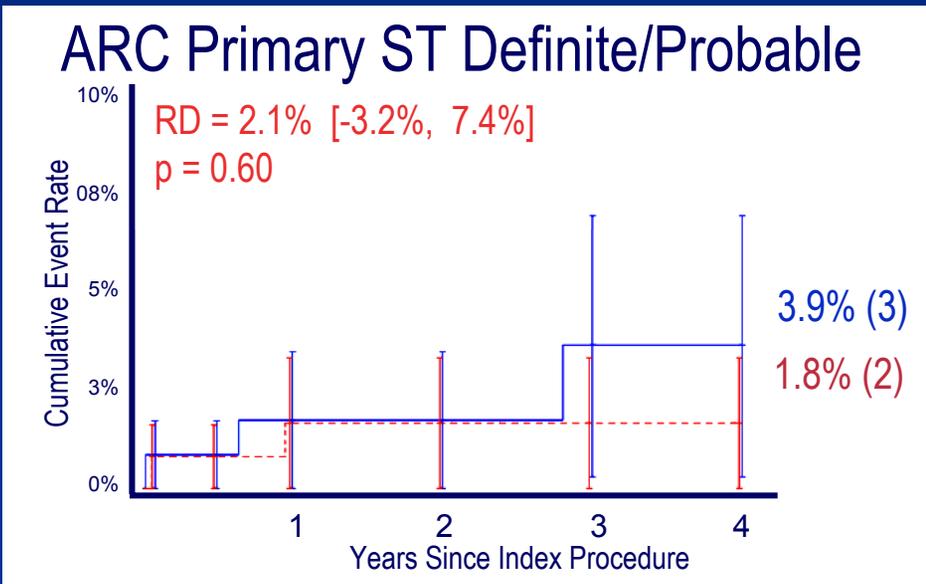
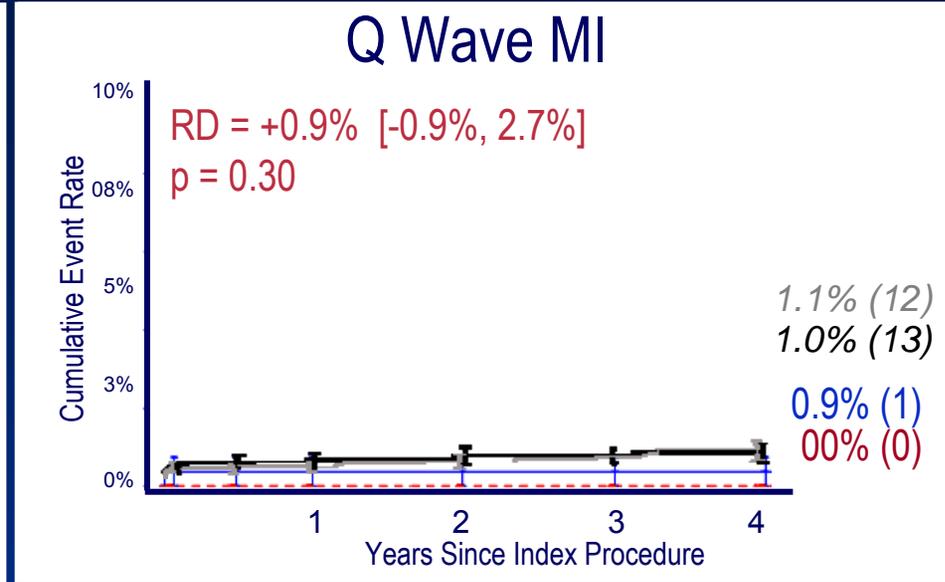
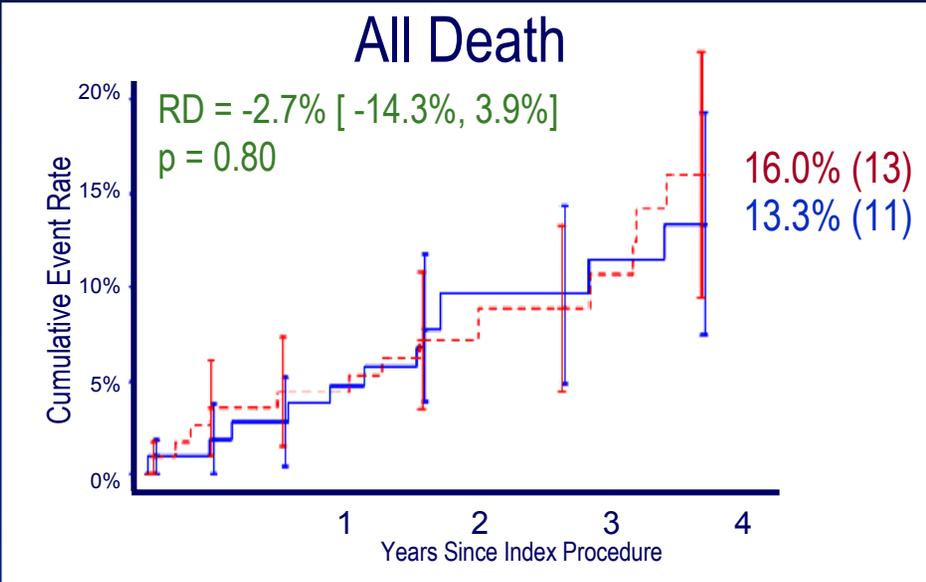
Taxus Subgroup Analysis

Insulin-Requiring Diabetics (N = 221)

— TAXUS (N=107) — BMS (N=114)

RD = Rate Difference = TAXUS — BMS

No increase Increase



TAXUS Insulin-Requiring Diabetics (N=221)

Annual Event Rates

Δ = Rate Difference = TAXUS — BMS
 No increase (green)
 Increase (red)

Event	0-1 Year (% / patient-year)				1-4 Years (% / patient-year)				4-year Cumulative Rates (K-M estimate [%])			
	Taxus	BMS	Rate Difference		Taxus	BMS	Rate Difference		Taxus	BMS	Rate Difference	
			Δ	p			Δ	p			Δ	p
All Death	2.89	4.54	-1.65	0.53	4.06	3.85	0.21	0.89	13.3	16.0	-2.7	0.80
Cardiac Death	1.93	3.63	-1.71	0.46	2.03	0.96	1.07	0.36	6.9	6.4	0.5	0.90
All MI	4.00	6.61	-2.60	0.42	1.02	0.48	0.54	0.53	7.8	8.3	-0.5	0.66
QWMI	0.97	0.00	0.97	0.30	0.00	0.00	0.00	NE	0.9	0.0	0.9	0.30
ST Protocol	0.96	0.91	0.06	0.96	0.51	0.00	0.51	0.31	3.0	0.9	2.1	0.53
Total ARC ST All	2.90	2.73	0.17	0.94	1.53	0.96	0.57	0.59	6.9	3.6	3.3	0.45
TLR	7.96	19.70	-11.74	0.02	2.60	2.98	-0.37	0.86	12.8	23.7	-10.9	0.03
TVR-CABG	4.89	1.84	3.05	0.22	1.03	0.97	0.05	0.95	7.8	5.9	1.9	0.31

p-value from Log rank test of no difference in the Kaplan-Meier curves between groups

TAXUS Small Vessels RVD ≤ 2.5 mm Visual (N = 965)

Annual Event Rates

Δ = Rate Difference = TAXUS — BMS
 No increase (green)
 Increase (red)

Event	0-1 Year (% / patient-year)			
	Taxus	BMS	Rate Difference	
			Δ	p
All Death	1.95	2.30	-0.35	0.71
Cardiac Death	1.52	1.46	0.05	0.95
All MI	3.35	5.63	-2.29	0.10
QWMI	0.22	0.63	-0.41	0.33
ST Protocol	0.43	1.05	-0.62	0.28
Total ARC ST All	1.52	2.10	-0.58	0.51
TLR	11.77	25.08	-13.31	<0.0001
TVR-CABG	1.96	6.26	-4.30	0.001

1-4 Years (% / patient-year)			
Taxus	BMS	Rate Difference	
		Δ	p
2.17	1.60	0.57	0.37
0.68	0.75	-0.06	0.87
1.04	0.76	0.28	0.53
0.11	0.11	0.01	0.98
0.23	0.00	0.23	0.14
0.80	0.96	-0.16	0.71
1.62	3.22	-1.60	0.03
0.69	1.30	-0.61	0.20

4-year Cumulative Rates (K-M estimate [%])			
Taxus	BMS	Rate Difference	
		Δ	p
7.9	7.3	0.6	0.63
3.3	3.7	-0.4	0.95
6.8	7.4	-0.6	0.28
0.4	0.8	-0.4	0.44
1.1	1.0	0.1	0.79
3.7	4.4	-0.7	0.56
14.5	27.7	-13.2	<0.0001
5.0	10.1	-5.1	0.0006

p-value from Log rank test of no difference in the Kaplan-Meier curves between groups

TAXUS Long Lesions $\geq 28\text{mm}$ (N = 341)

Annual Event Rates

Δ = Rate Difference = TAXUS — BMS
 No increase (green)
 Increase (red)

Event	0-1 Year (% / patient-year)				1-4 Years (% / patient-year)				4-year Cumulative Rates (K-M estimate [%])			
	Taxus	BMS	Rate Difference		Taxus	BMS	Rate Difference		Taxus	BMS	Rate Difference	
			Δ	p			Δ	p			Δ	p
All Death	2.33	3.77	-1.44	0.45	1.59	2.60	-1.01	0.44	7.7	10.7	-3.0	0.28
Cardiac Death	2.33	1.88	0.45	0.78	1.19	0.43	0.76	0.36	5.5	2.5	3.0	0.44
All MI	9.49	3.22	6.28	0.03	1.62	0.87	0.75	0.46	15.1	5.6	9.5	0.01
QWMI	1.77	0.63	1.14	0.35	0.00	0.00	0.00	NE	1.7	0.6	1.1	0.35
ST Protocol	0.58	0.63	-0.05	0.96	0.00	0.00	0.00	NE	0.6	0.6	0.0	0.96
Total ARC ST All	1.76	2.52	-0.77	0.63	1.20	0.87	0.33	0.72	6.6	5.5	1.1	0.90
TLR	9.71	29.83	-20.12	<0.0001	2.46	4.63	-2.17	0.23	13.1	31.3	-18.2	<0.0001
TVR-CABG	1.18	4.48	-3.31	-0.07	0.40	1.76	-1.36	0.15	1.8	8.7	-6.9	0.02

TAXUS Multiple Stents in Single Vessels (N = 497)

Annual Event Rates

Δ = Rate Difference = TAXUS — BMS
 No increase (green)
 Increase (red)

Event	0-1 Year (% / patient-year)				1-4 Years (% / patient-year)				4-year Cumulative Rates (K-M estimate [%])			
	Taxus	BMS	Rate Difference		Taxus	BMS	Rate Difference		Taxus	BMS	Rate Difference	
			Δ	p			Δ	p			Δ	p
All Death	1.60	2.12	-0.51	0.68	1.16	2.77	-1.61	0.13	7.4	11.4	-4.0	0.16
Cardiac Death	1.20	1.27	-0.07	0.95	0.58	0.00	0.58	0.17	3.5	1.3	2.2	0.53
All MI	9.63	6.65	2.98	0.30	0.58	1.25	-0.67	0.37	9.5	11.4	-1.9	0.53
QWMI	0.81	1.28	-0.47	0.61	0.00	0.31	-0.31	0.30	0.8	3.2	-2.4	0.37
ST Protocol	1.21	0.85	0.36	0.70	0.00	0.00	0.00	NE	1.2	0.8	0.4	0.70
Total ARC ST All	2.02	2.12	-0.10	0.94	0.29	0.31	-0.02	0.97	2.4	2.5	-0.1	0.93
TLR	11.80	33.98	-22.19	<0.0001	2.05	4.87	-2.82	0.06	12.8	35.9	-23.1	<0.0001
TVR-CABG	2.45	4.76	-2.31	0.18	0.88	1.88	-1.00	0.28	5.0	10.3	-5.3	0.08

p-value from Log rank test of no difference in the Kaplan-Meier curves between groups

EVENT HAZARD RATES - FIRST YEAR

TAXUS By Subgroups

Event	Overall N =2797	Diabetics N =715	Insulin-requiring diabetics N =221	RVD \leq 2.5mm N = 965	Lesions \geq 28mm N =341	Multiple stents N=497
All Death	1.97	2.60	2.89	1.95	2.33	1.60
Cardiac Death	1.10	1.73	1.93	1.52	2.33	1.20
All MI	4.24	3.57	4.00	3.35	9.49	9.63
QWMI	0.66	0.29	0.97	0.22	1.77	0.81
ST Protocol	0.73	0.58	0.96	0.43	0.58	1.21
Primary ARC ST Def/ Prob	0.88	0.87	1.93	0.65	1.17	1.62
TLR	7.37	8.95	7.96	11.77	9.71	11.80
TVR-CABG	1.69	2.62	4.89	1.96	1.18	2.45

EVENT HAZARD RATES - FIRST YEAR

BMS By Subgroups

Event	Overall N =2797	Diabetics N =715	Insulin-requiring diabetics N =221	RVD _≤ 2.5mm N = 965	Lesions _≥ 28mm N =341	Multiple stents N=497
All Death	1.90	2.84	4.54	2.30	3.77	2.12
Cardiac Death	1.31	1.99	3.63	1.46	1.88	1.27
All MI	4.76	6.28	6.61	5.63	3.22	6.65
QWMI	0.37	0.57	0.00	0.63	0.63	1.28
ST Protocol	0.66	1.43	0.91	1.05	0.63	0.85
Primary ARC ST Def/ Prob	0.73	1.43	1.82	1.47	1.26	1.28
TLR	17.59	21.81	19.70	25.08	29.83	33.98
TVR-CABG	3.19	4.67	1.84	6.26	4.48	4.76

ANNUAL HAZARD RATES - YEARS 1-4

TAXUS - By Subgroup

Event	Overall N =2797	Diabetics N =715	Insulin-requiring diabetics N =221	RVD \leq 2.5mm N = 965	Lesions \geq 28mm N =341	Multiple stents N=497
All Death	1.71	2.52	4.06	2.17	1.59	1.16
Cardiac Death	0.57	1.11	2.03	0.68	1.19	0.58
All MI	1.01	1.28	1.02	1.04	1.62	0.58
QWMI	0.18	0.00	0.00	0.11	0.00	0.00
ST Protocol	0.21	0.16	0.51	0.23	0.00	0.00
Primary ARC ST Def/ Prob	0.32	0.32	0.51	0.34	0.40	0.00
TLR	1.57	2.09	2.60	1.62	2.46	2.05
TVR-CABG	0.47	0.95	1.03	0.69	0.40	0.88

ANNUAL HAZARD RATES - YEARS 1-4

BMS - By Subgroup

Event	Overall N =2797	Diabetics N =715	Insulin-requiring diabetics N =221	RVD \leq 2.5mm N = 965	Lesions \geq 28mm N =341	Multiple stents N=497
All Death	1.87	2.70	3.85	1.60	2.60	2.77
Cardiac Death	0.60	0.60	0.96	0.75	0.43	0.00
All MI	0.71	0.61	0.48	0.76	0.87	1.25
QWMI	0.25	0.15	0.00	0.11	0.00	0.31
ST Protocol	0.04	0.00	0.00	0.00	0.00	0.00
Primary ARC ST Def/ Prob	0.11	0.00	0.00	0.00	0.44	0.00
TLR	2.34	2.46	2.98	3.22	4.63	4.87
TVR-CABG	1.04	1.37	0.97	1.30	1.76	1.88

ANNUAL EVENT RATE difference signals (Taxus – BMS) Year 1 By Subgroup

Event	Overall N =2797	Diabetics N =715	Insulin-requiring diabetics N =221	RVD≤ 2.5mm N = 965	Lesions ≥ 28mm N =341	Multiple stents N=497
All Death	0.08 p=0.89	-0.25 p=0.84	-1.65 p=0.53	-0.35 p=0.71	-1.44 p=0.45	-0.51 p=0.68
Cardiac Death	-0.22 p=0.60	-0.26 p=0.80	-1.71 p=0.46	0.05 p=0.95	0.45 p=0.78	-0.07 p=0.95
All MI	-0.51 p=0.52	-2.72 p=0.12	-2.60 p=0.42	-2.29 p=0.10	6.28 p=0.03	2.98 P=0.30
QWMI	0.30 p=0.52	-0.28 p=0.57	0.97 p=0.30	-0.41 p=0.33	1.14 p=0.35	-0.47 p=0.61
ST Protocol	-0.07 p=0.88	-0.86 p=0.27	0.06 P=0.96	-0.62 p=0.28	-0.77 p=0.63	0.36 p=0.70
Primary ARC ST Def/ Prob	0.07 p=0.83	-0.57 p=0.49	0.12 P=0.95	-0.82 P=0.23	-0.09 p=0.94	0.34 p=0.76
TLR	-10.21 p<0.0001	-12.86 p<0.0001	-11.74 p=0.02	-13.31 p<0.0001	-20.12 p<0.0001	-22.19 p<0.0001
TVR-CABG	-1.50 p=0.01	-2.05 p=0.16	3.05 p=0.22	-4.30 p=0.001	-3.31 p=0.07	-2.31 P=0.18

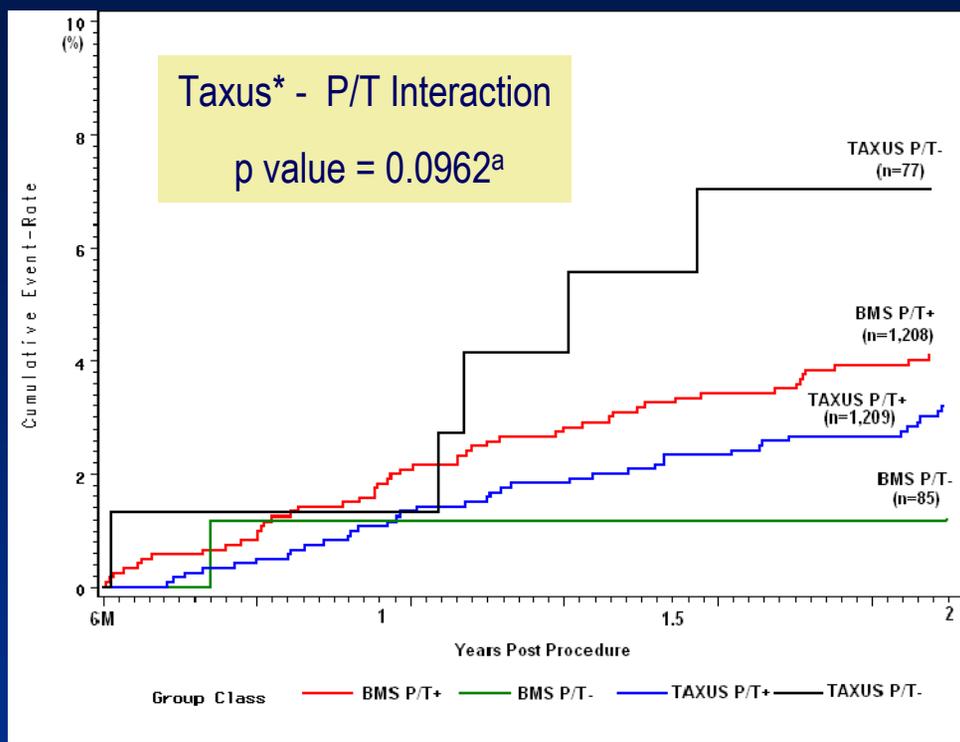
ANNUAL EVENT RATE difference signals (Taxus – BMS) Years 1-4 By Subgroup

Event	Overall N =2797	Diabetics N =715	Insulin-requiring diabetics N =221	RVD \leq 2.5mm N = 965	Lesions \geq 28mm N =341	Multiple stents N=497
All Death	-0.16 p=0.65	-0.18 p=0.85	0.21 p=0.89	0.57 p=0.37	-1.01 p=0.44	-1.61 p=0.13
Cardiac Death	-0.03 p=0.88	0.50 p=0.33	1.07 p=0.36	-0.06 p=0.87	0.76 p=0.36	0.58 p=0.17
All MI	-0.3 p=0.23	0.68 p=0.21	0.54 p=0.53	0.28 p=0.53	0.75 p=0.46	-0.67 P=0.37
QWMI	-0.07 p=0.57	-0.15 p=0.34	0.00 NE	0.01 p=0.98	0.00 NE	-0.31 p=0.30
ST Protocol	0.18 p=0.06	0.16 p=0.30	0.51 P=0.31	0.23 p=0.14	0.33 p=0.72	0.00 NE
Primary ARC ST Def/ Prob	0.22 p=0.08	0.32 p=0.14	0.51 P=0.30	0.34 p=0.07	-0.03 p=0.96	0.00 NE
TLR	-0.77 p=0.04	-0.37 p=0.66	-0.37 p=0.86	-1.60 p=0.03	-2.17 P=0.23	-2.82 p=0.06
TVR-CABG	-0.57 p=0.01	-0.41 p=0.53	0.05 p=0.95	-0.61 p=0.20	-1.36 p=0.15	-1.00 p=0.28

CUMULATIVE TOTAL EVENT Differences Years 0-4 By Subgroup (Taxus – BMS)

Event	Overall N =	Diabetics N =	Insulin-requiring diabetics N =	RVD \leq 2.5mm N =	Lesions \geq 28mm N =	Multiple stents N =
All Death	-0.3 p=0.78	-1.5 p=0.78	-2.7 p=0.80	0.6 p=0.63	-3.0 p=0.28	-4.0 p=0.16
Cardiac Death	-0.4 p=0.64	1.0 p=0.64	0.5 p=0.90	-0.4 p=0.95	3.0 p=0.44	2.2 p=0.53
All MI	0.5 p=0.87	-0.2 p=0.57	-0.5 p=0.66	-0.6 p=0.28	9.5 p=0.01	-1.9 p=0.53
QWMI	-0.1 p=0.83	-0.8 p=0.34	0.9 p=0.30	-0.4 p=0.44	1.1 p=0.35	-2.4 p=0.37
ST Protocol	0.5 p=0.24	-0.2 p=0.50	2.1 p=0.53	0.1 p=0.79	0.0 p=0.96	0.4 p=0.70
Primary ARC ST Def/ Prob	0.7 p=0.17	0.8 p=0.96	2.1 p=0.60	0.1 p=0.83	-0.3 p=0.93	0.4 p=0.76
TLR	-9.7 p<0.0001	-11.5 p<0.0001	-10.9 p=0.03	-13.2 p<0.0001	-18.2 p<0.0001	-23.1 p<0.0001
TVR-CABG	-3.1 p=0.0004	-2.6 p=0.13	1.9 p=0.31	-5.1 p=0.0006	-6.9 p=0.02	-5.3 p=0.08

Death or MI During Follow-up to 2 Years Post-Procedure According to Plavix® /Ticlid® Usage at 6 Months



(n=2,522)		Plavix/Ticlid Use Overtime			ASA Use Overtime		
Group	n	6 M Landmark	12 M [†]	24 M [*]	6 M Landmark [†]	12 M [†]	24 M [*]
BMS P/T+	1208	100%	49.5%	46.6%	98.1%	95.3%	96.3%
BMS P/T-	85	-	-	-	-	-	-
TAXUS P/T+	1209	100%	49.2%	43.3%	98.0%	94.3%	94.9%
TAXUS P/T-	77	-	-	-	-	-	-

[†] Medication data available in TAXUS 2, 4, and 5

^{*} Medication data available in TAXUS 4, 5 only

a. adjusted Cox regression model, additionally adjusted for patient baseline and lesion characteristics

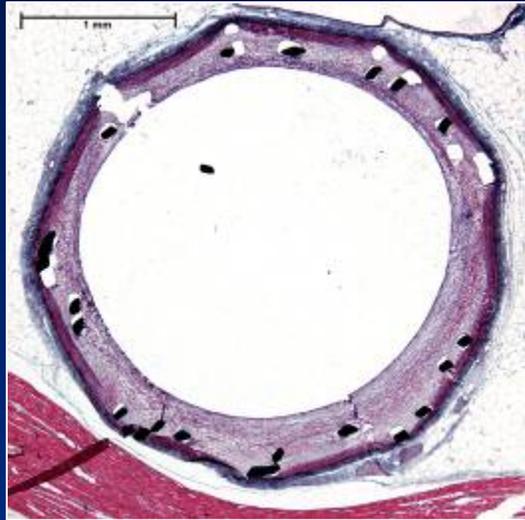
Plavix and Ticlid are trademarks of Sanofi-Aventis

Translute™ Vascular Compatibility

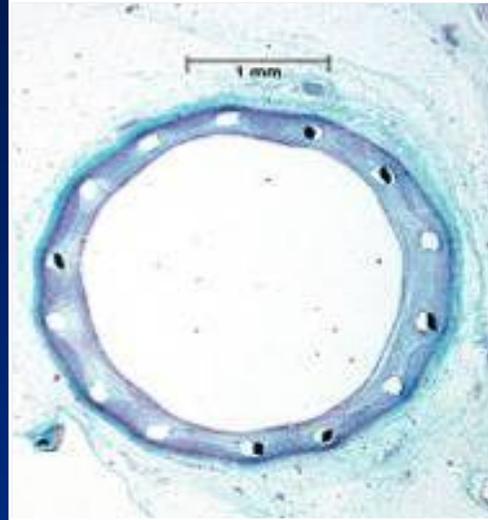
Porcine Coronary, SIBS coated Stents

**Bare
Stent**

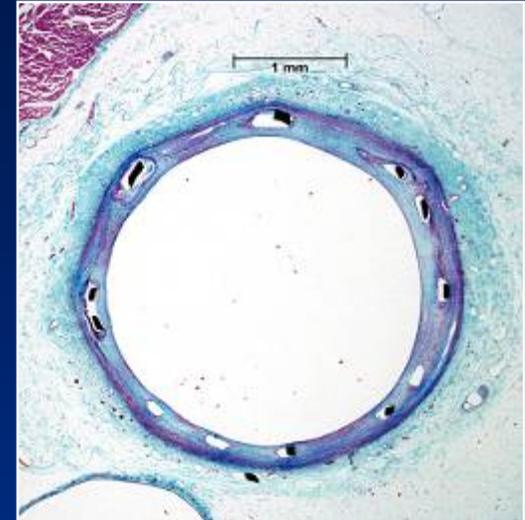
30d



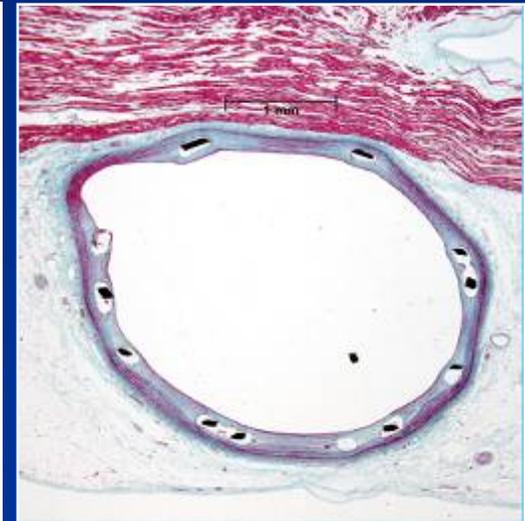
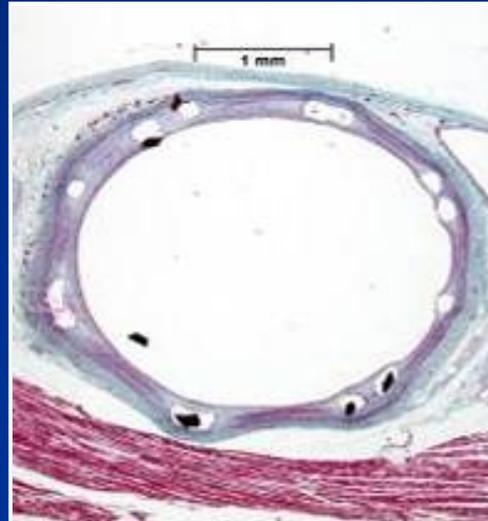
90d



180d



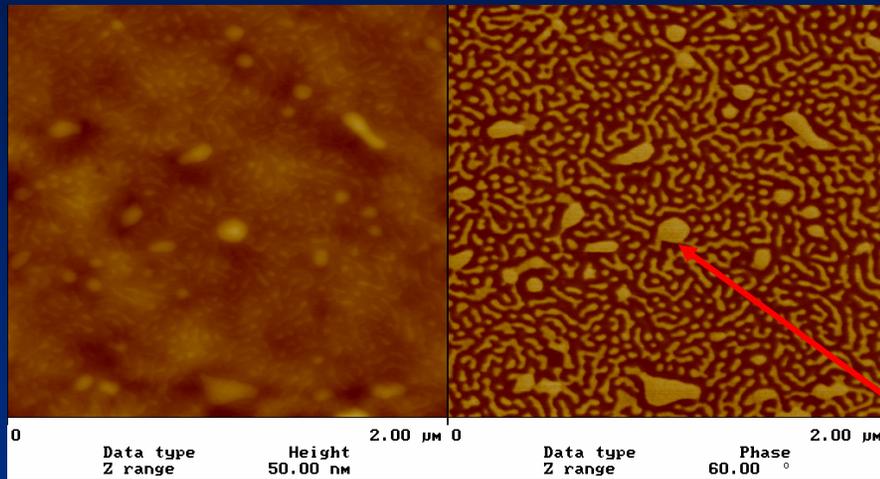
**Translute
Coated
Stent
(no paclitaxel)**



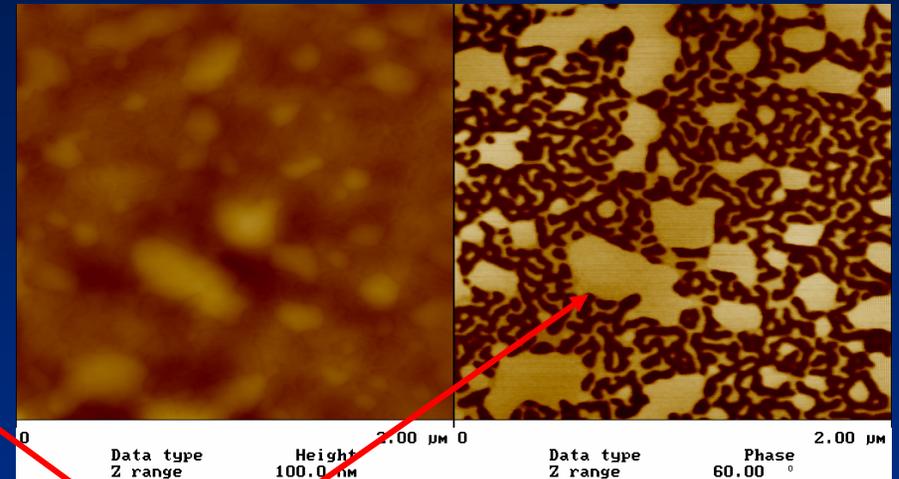
In collaboration with Dr. Rob Schwartz (Mayo Clinic) and Dr. Greg Wilson (Sick Children's-Toronto)

AFM Images of TAXUS Stents of Varying Formulations

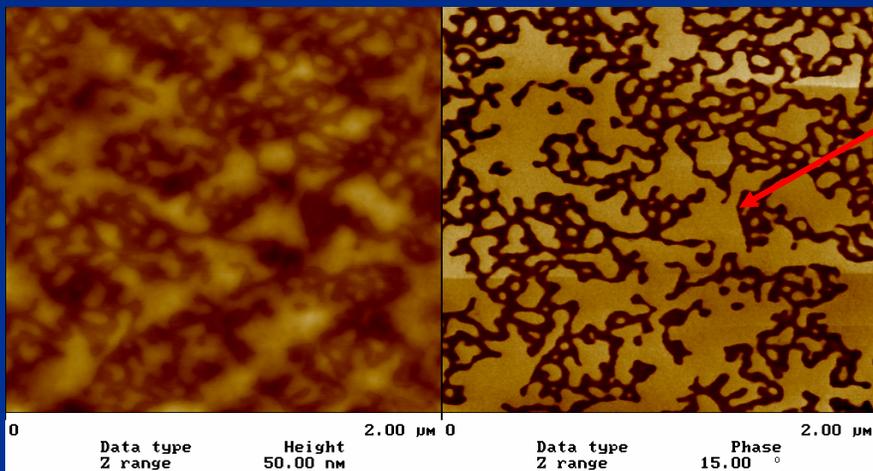
8.8% PTx (SR formulation)



25% PTx (MR formulation)



35% PTx (FR formulation)

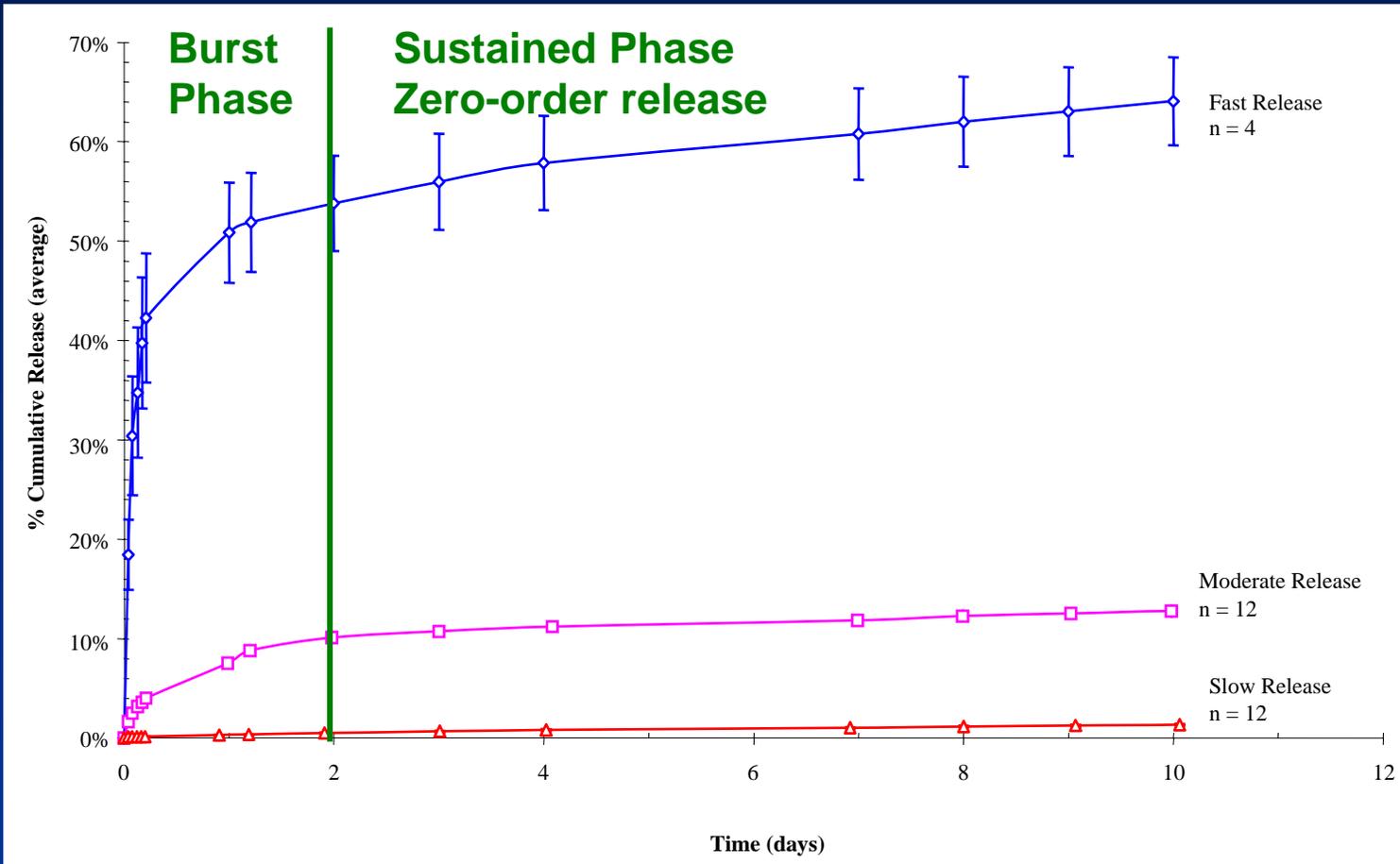


PTx Particles

Increasing PTx concentration results in a more saturated matrix with more drug:drug interaction

Modulating Drug Release

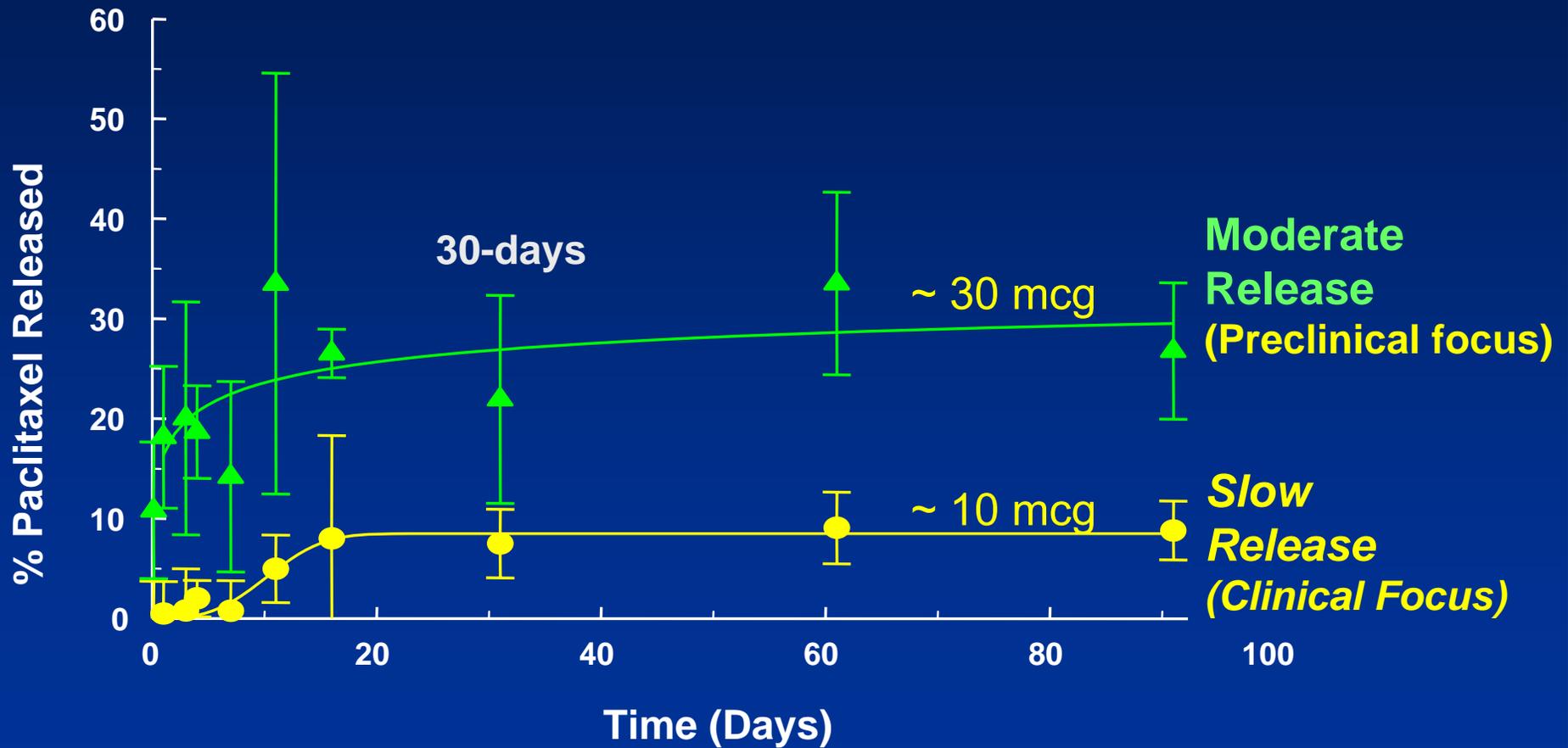
Altering drug to polymer ratio to effect drug release and biological response



Release Media - Physiological Saline w/ surfactant - pH 7.4 @ 37°C

Formulation in **Translute™** controls both drug release amount as well as time course

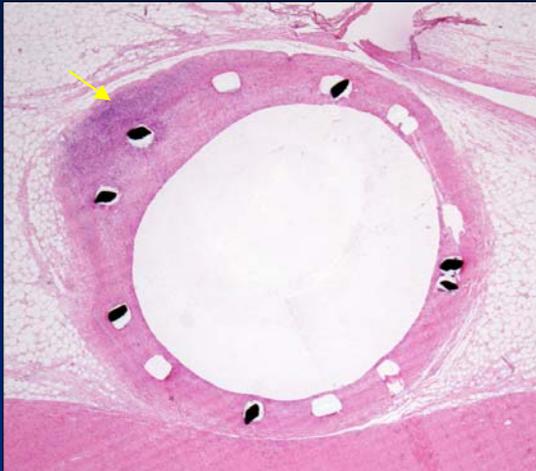
Rabbit Iliac Cumulative Release
Plateau after 30 days



CYPHER vs TAXUS Stents:
Comparing the Inflammatory Response
in Porcine Coronary Arteries

Robert S. Schwartz and Gregory J. Wilson

Regional Patterns of Severe Inflammation (SI)



1520 LCX-4

X 20

Severe Unifocal



1517 LCX-3

X 20

Severe Multifocal



1517 LCX-4

X 20

Severe Circumferential

Unifocal: One focus of SI involving no more than one quadrant (90°) of the circumference

Multifocal: Two or more foci of SI involving no more than 3 quadrants (270° maximum) of the circumference

Circumferential: Several foci of SI involving 4 quadrants of the circumference (usually every strut involved)

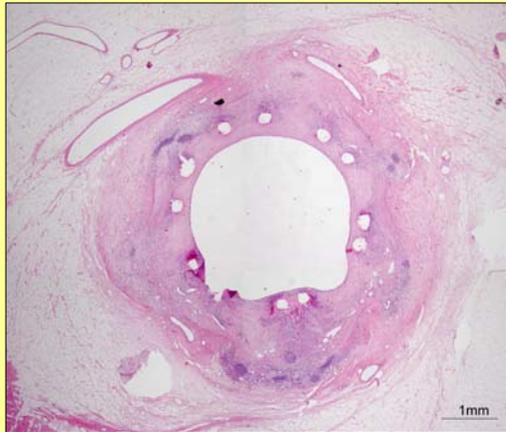
CYPHER vs TAXUS Comparison of Circumferential Severe Inflammation (CSI) – X3

Proximal*

Overlap*

Distal*

CYPHER
CSI – X3
43.1%
(25/58)



4P590 RCA-B



4P590 RCA-C



4P590 RCA-D

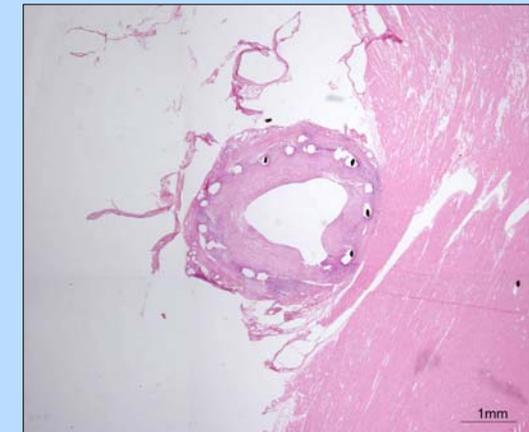
TAXUS
CSI – X3
1.7%
(1/58)



1569 LAD-2



1569 LAD-3



1569 LAD-4

*20X magnification

Circumferential Severe Inflammation (CSI)- X3 All Studies Combined

Duration	CYPHER (%)	TAXUS (%)	<i>P</i> -Value*
30 Days	0.0 (0/24)	0.0 (0/24)	1.0
90 Days	52.3 (11/21)	5.0 (1/20)	0.0014
180 Days	60.9 (14/23)	0.0 (0/24)	< 0.0001

Significant increase over time in prevalence of CSI-X3[†] in CYPHER between 30 & 90 days
(*P*=0.0008)

No significance difference over time in CYPHER between 90 & 180 days (*P*=0.27)

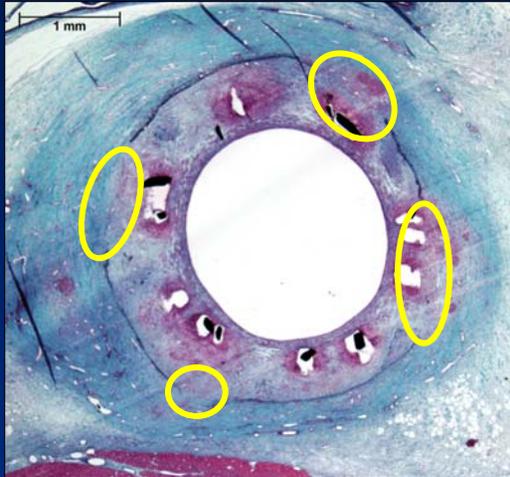
Prevalence of CSI-X3 in CYPHER significantly greater than TAXUS
at 90 & 180 days

[†]Circumferential severe inflammation in all 3 sections

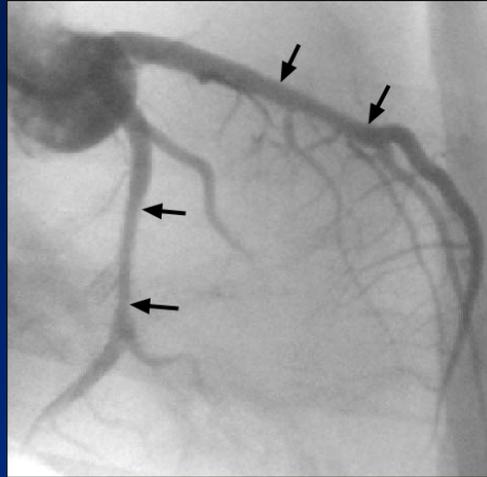
*Fisher's Exact Test-Two Tailed

Angiography Compared With Histology

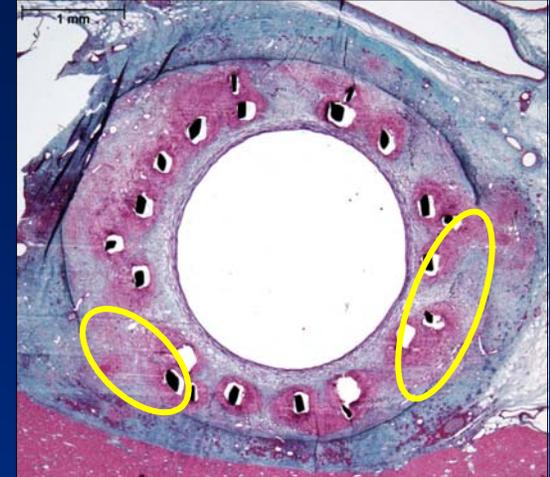
Two DES Pairs



1502 LCX (overlap section) X 20



Animal 1502 (CYPHER)



1502 LAD (overlap section) X 20

90-Day Angiogram

- Modest narrowing of both CYPHER stents
- No insight into existing inflammation

90-Day Histology

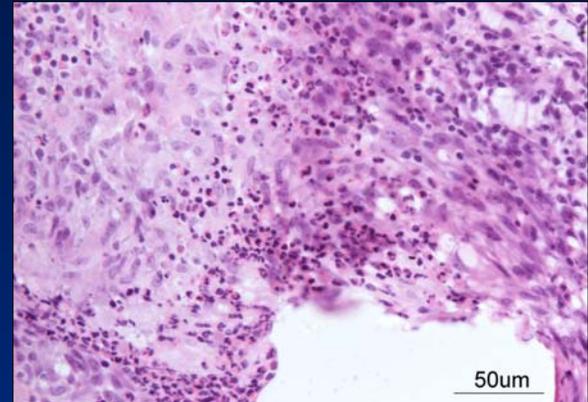
- Circumferential severe inflammation across 3 sections
- Substantial breakdown of black elastica (encircled)

Severe Inflammation Uncommon with either Bare Metal Control



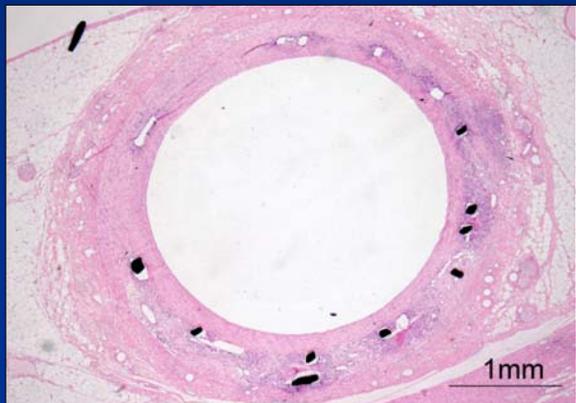
1517 LAD-2

BX Sonic
@ 90 days



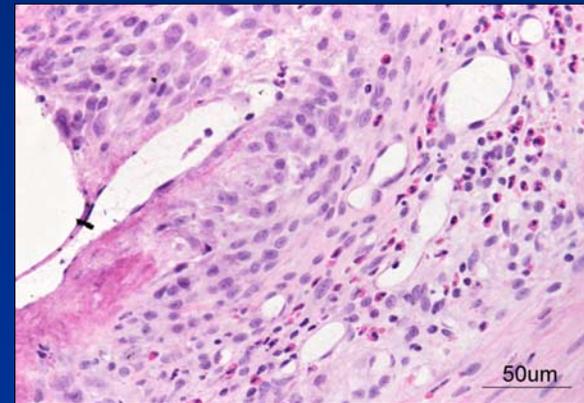
1517 LAD-2

Across Combined BX Velocity & BX Sonic: 2.7% (1/37) CSI-X3*



1583 LAD-3

Liberté
@ 90 days



1583 LAD-3

Across Combined Express & Liberté : 1.9% (1/52) SI-X2*

*CSI-X3: Circumferential severe inflammation in all 3 sections; SI-X2: Severe inflammation in 2 sections