

**XIENCE™ V Everolimus
Eluting Coronary Stent
System (EECSS)**

PMA # P070015

Gary C. Johnson

Vice President, Regulatory Affairs, Clinical Research
and Quality Assurance, Abbott Vascular

Agenda

- Introduction
 - Gary Johnson, Vice President, Abbott Vascular
- XIENCE V Technology
 - Murthy Simhambhatla, PhD, Vice President, Abbott Vascular
- XIENCE V Pre-clinical Program Overview
 - Leslie Coleman, DVM, Director, Abbott Vascular
- XIENCE V Clinical Program Overview and Results
 - Gregg Stone, MD, Professor of Medicine, Columbia University
- XIENCE V Safety Overview
 - Mitchell Krucoff, MD, Professor of Medicine, Duke University Medical Center
- Conclusion
 - Krishna Sudhir, MD, PhD, Director, Abbott Vascular

Expert Consultants

- Stuart Pocock, PhD
 - London School of Hygiene and Tropical Medicine, Professor of Medical Statistics
- Alexandra Lansky, MD
 - Cardiovascular Research Foundation, Angiographic Core Lab
- Peter Fitzgerald, MD, PhD
 - Stanford University, IVUS Core Lab
- Renu Virmani, MD
 - CVPPath Institute, Inc., Medical Director
- Ronald Van Valen
 - Novartis, Drug Regulatory Affairs, Immunology and Infectious Diseases, Director

Purpose

- Review XIENCE V Design Goals
- Review XIENCE V comprehensive Pre-Clinical program
- Demonstrate that XIENCE V clinical data in its totality, establishes a reasonable assurance of safety and effectiveness, based on valid scientific evidence
- Review the XIENCE V Post-Approval clinical strategy that augments the Pre-Approval data and is effectively powered to evaluate low frequency events

XIENCE V

Proposed Indication for Use

The XIENCE V Everolimus Eluting Coronary Stent System (EECSS) is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to *de novo* native coronary artery lesions (length \leq 28 mm) with reference vessel diameters of 2.5 mm to 4.25 mm.

XIENCE V System Sizes

Diameters: 2.5, 2.75, 3.0, 3.5, 4.0 mm

Lengths: 8 – 28 mm

Platforms: RX and OTW

Length (mm)

	8	12	15	18	23	28
Diameter (mm)	✓	✓	✓	✓	✓	✓
2.5	✓	✓	✓	✓	✓	✓
2.75	✓	✓	✓	✓	✓	✓
3.0	✓	✓	✓	✓	✓	✓
3.5	✓	✓	✓	✓	✓	✓
4.0	✓	✓	✓	✓	✓	✓

Drug dose density: 100 $\mu\text{g}/\text{cm}^2$ for all sizes

XIENCE V

Major Design Components

- Stent and Delivery System:
 - MULTI-LINK VISION[®] & MULTI-LINK MINI VISION[®] Coronary Stent Systems (P020047 & P020047/S003)
- Drug Matrix:
 - Fluorinated Copolymer: PVDF-HFP (approved for use in other vascular applications)
- Drug:
 - Everolimus (Novartis Pharmaceutical Corporation)
 - Novartis has received 2 approvable letters from FDA
 - Novartis has granted FDA right to reference IND/NDA

XIENCE V

Marketing History

- XIENCE V has received regulatory approval and is marketed in 64 countries outside the US

XIENCE V

Regulatory/Clinical Strategy

- Abbott Vascular worked collaboratively with FDA in 2004 and 2005 to develop the SPIRIT III pivotal clinical trial design
- At the time of initiation of SPIRIT III (May 2005), FDA agreed the pivotal clinical trial and supporting clinical data in the XIENCE V SPIRIT clinical trial program would provide adequate assurance of safety and effectiveness for the XIENCE V Everolimus Eluting Coronary Stent System

XIENCE V

Regulatory/Clinical Strategy

- FDA has reviewed the everolimus safety pharmacology, toxicology and ADME studies and has identified no concerns
- FDA considers everolimus to be a well characterized and studied drug therefore, **not a New Molecular Entity (NME)**
- Since everolimus is not an NME, the requirement for 2,000 treated patients in clinical studies with a NME did not apply to the XIENCE V Clinical Program

Integrated Pre-Approval and Post-Approval Clinical Program (N > 16,000)

Pre-approval Clinical Data

SPIRIT First

RCT 1:1 XIENCE V vs. VISION (n = 60) OUS

SPIRIT II

RCT 3:1 XIENCE V vs. TAXUS[®] (n = 300) OUS

SPIRIT III

RCT 2:1 XIENCE V vs. TAXUS (n = 1,002) US

SPIRIT III 4.0

Registry 4.0 mm (n = 80) US

Ongoing and Planned Clinical Data

SPIRIT III Japan

Registry (n = 88) Japan

SPIRIT IV

RCT XIENCE V vs. TAXUS 2:1 Continued Access (n = 3,690) US

SPIRIT V

Registry (n = 2,700), RCT Diabetics 2:1 vs. TAXUS (n = 300) OUS

**XIENCE V
SPIRIT Women**

Registry (n = 1,550) RCT 2:1 vs. CYPHER[®] (n = 450) OUS

XIENCE V USA

Post-approval Registry – real world (n ~ 5,000) US

XIENCE India

Post-approval Registry – real world (n ~ 1,000) OUS

Integrated Pre-Approval and Post-Approval Clinical Program

- Pre-Approval Clinical Studies:
 - All Clinical trials met their pre-specified Primary and Major Secondary Endpoints
 - Showed Non-inferiority and Superiority in LL over BMS
 - Showed Non-inferiority and Superiority in LL over approved DES
 - Showed Non-inferiority in TVF compared to the TAXUS DES
 - Long term follow-up to 5 years
- Ongoing and Planned Clinical Studies:
 - Include real world patients
 - Powered to effectively evaluate low frequency events, 0.5%
 - Designed to potentially support label expansion
 - Long term follow-up to 5 years

SPIRIT II & SPIRIT III

2 Year Analysis

- Abbott Vascular has considered FDA panel comments in December 2006 and has also performed a safety subset analysis of all available 2 year data from SPIRIT II and SPIRIT III
- The results are consistent with the 1 year data from SPIRIT II and SPIRIT III as well as the 3 year data from SPIRIT FIRST

XIENCE V Technology

Murthy Simhambhatla, Ph.D.

Vice President and General Manager, DES

Abbott Vascular

XIENCE V Design Goal

Develop 2nd Generation DES

- Build on proven Multi-Link VISION and MINI VISION Bare Metal Stent (BMS) and Stent Delivery Systems
 - Flexible stent with thin struts
 - Proven deliverability
- Develop thin, biocompatible drug coating
 - Effective with low drug loading
 - Stable polymer
 - Uniform, conformal coating
 - Controlled and complete release of drug
 - Hemocompatibility and vascular compatibility

XIENCE V

Scientific Design & Integration

**MULTI-LINK VISION
Stent**



**MULTI-LINK VISION
Stent Delivery
System**

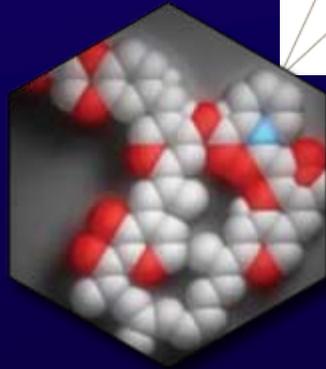


Deliverability

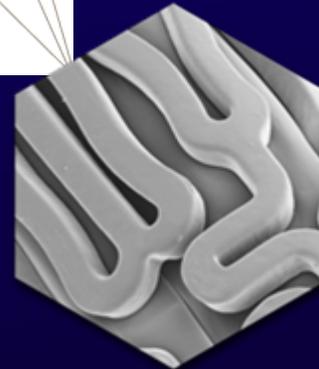
Efficacy

Safety

Everolimus



**Fluorinated
Copolymer**



XIENCE V

Built On The Proven VISION Stent Platform

Cobalt Chromium Technology

- Allows for thinner struts without compromise to radiopacity or radial strength¹



Thin Strut Stent Design

- Outstanding flexibility and conformability
- .0032" (81 μm) strut thickness²



Low System Profile

- Excellent deliverability



VISION Stent Delivery System

- Soft, highly flexible Pebax balloon material
- Short tapers

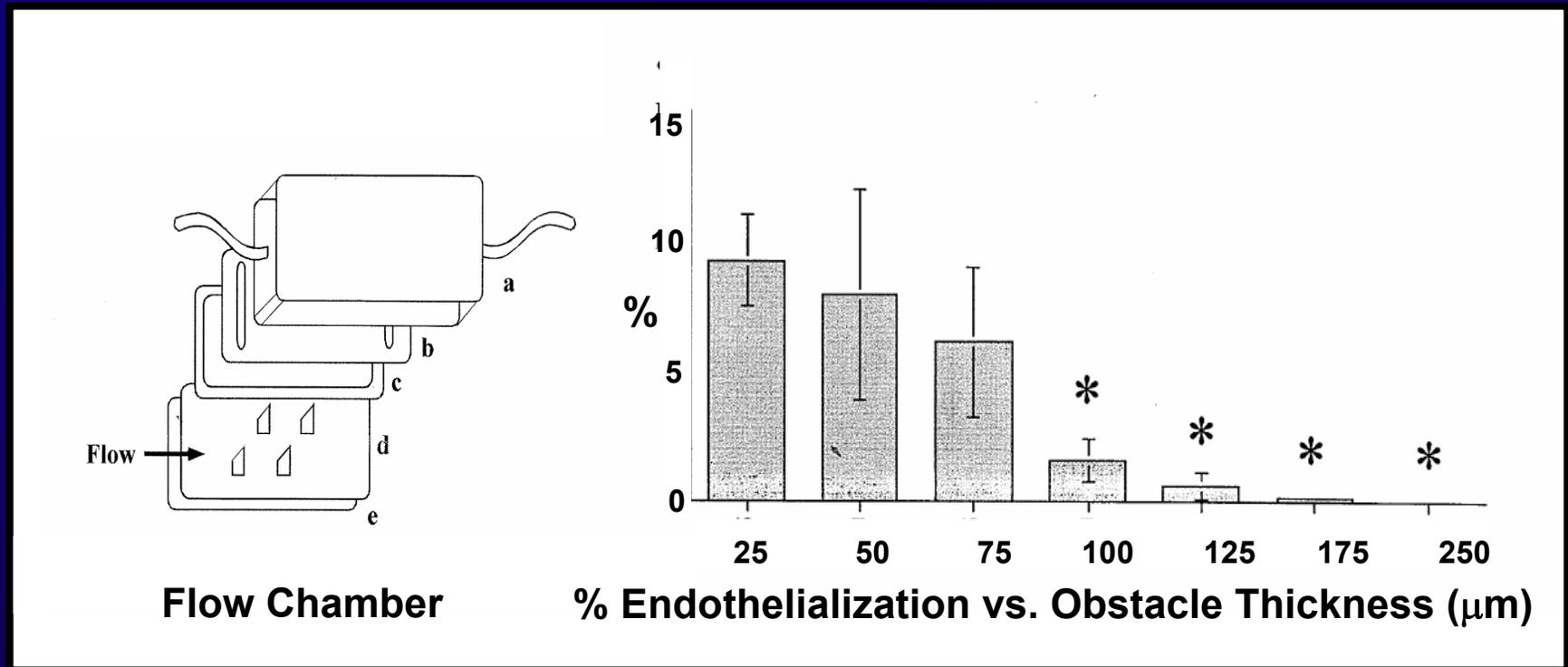


¹. As compared to stainless steel. Source: ASTM International.

². Tests performed by and data on file at Abbott Vascular.

SCIENCE V

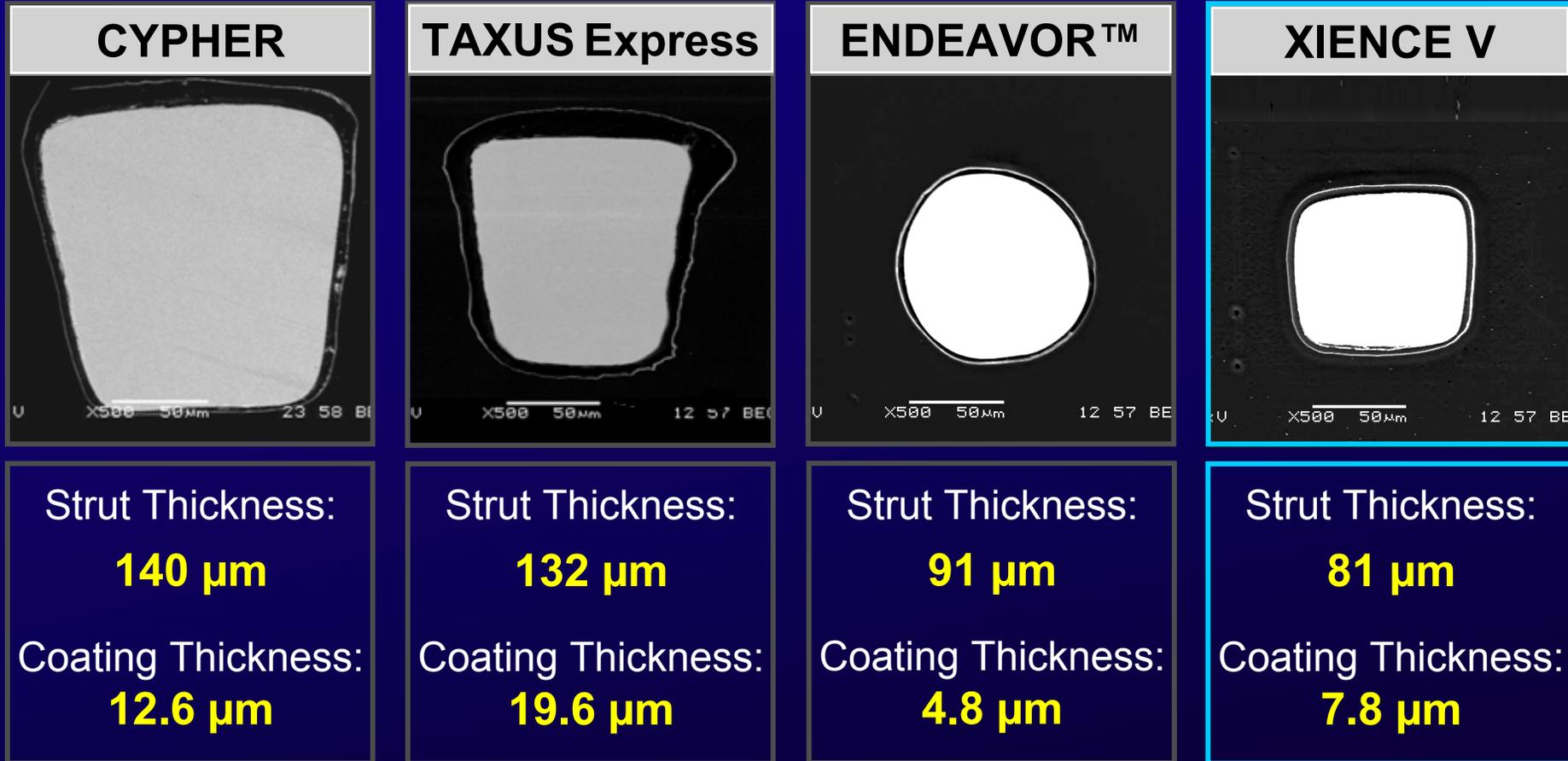
Endothelialization and strut thickness



Endothelial coverage may be impaired for thicker stent struts

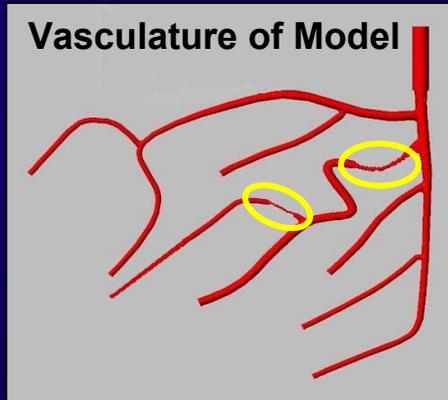
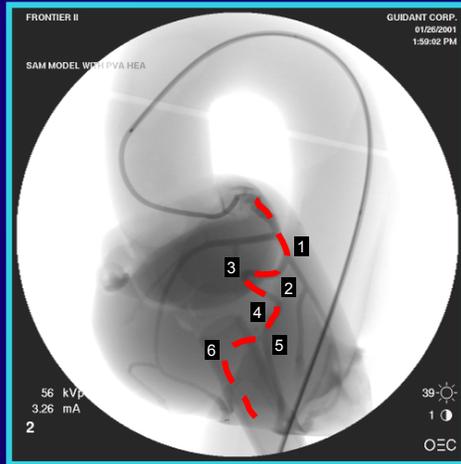
XIENCE V

Progression Towards Thinner Struts

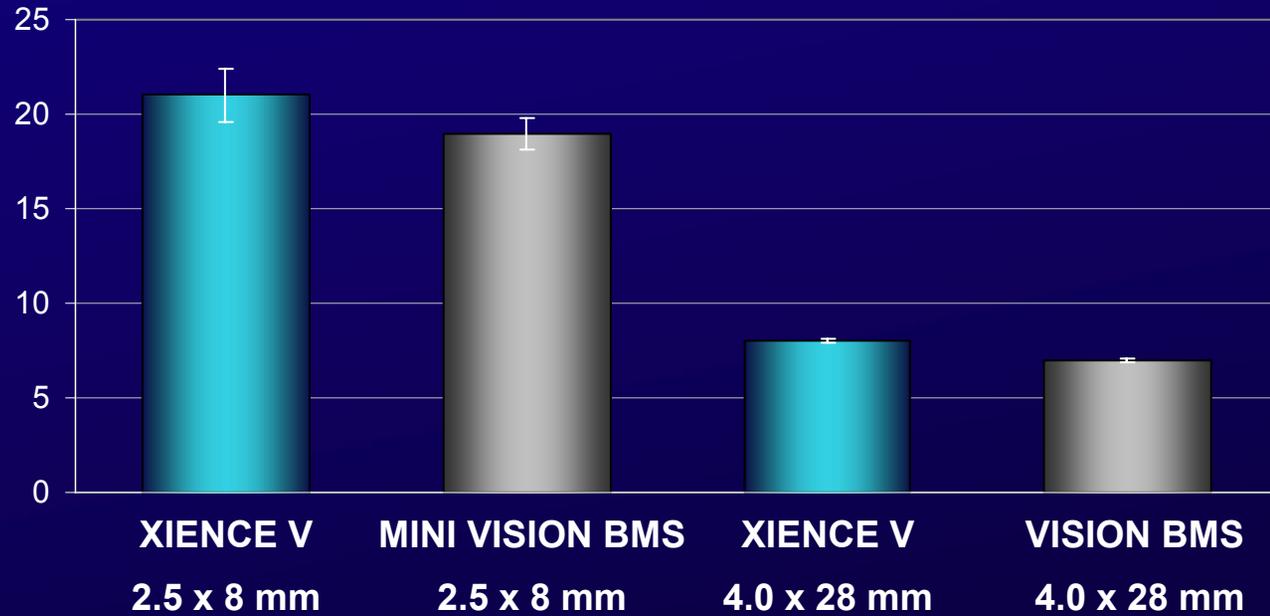


Abluminal coating thickness represented

XIENCE V Deliverability

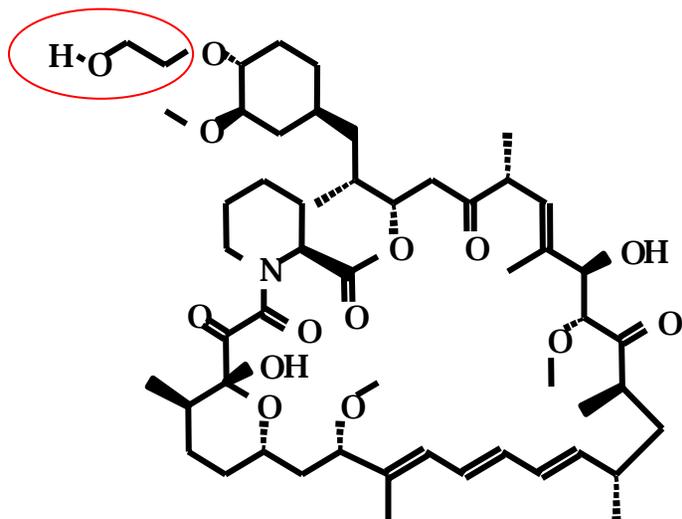


Deliverability Score

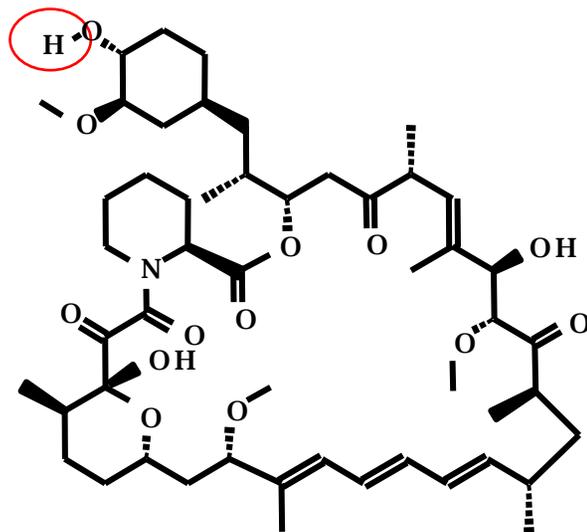


Maintains Deliverability of Proven VISION BMS

Everolimus



everolimus
 IC_{50} : 0.9-3.6 nM



sirolimus
 IC_{50} : 0.4-3.5 nM

IC_{50} values for Bovine SMCs
Schuler, W. et al., Transplantation, Vol. 64, 36-42, 1997.

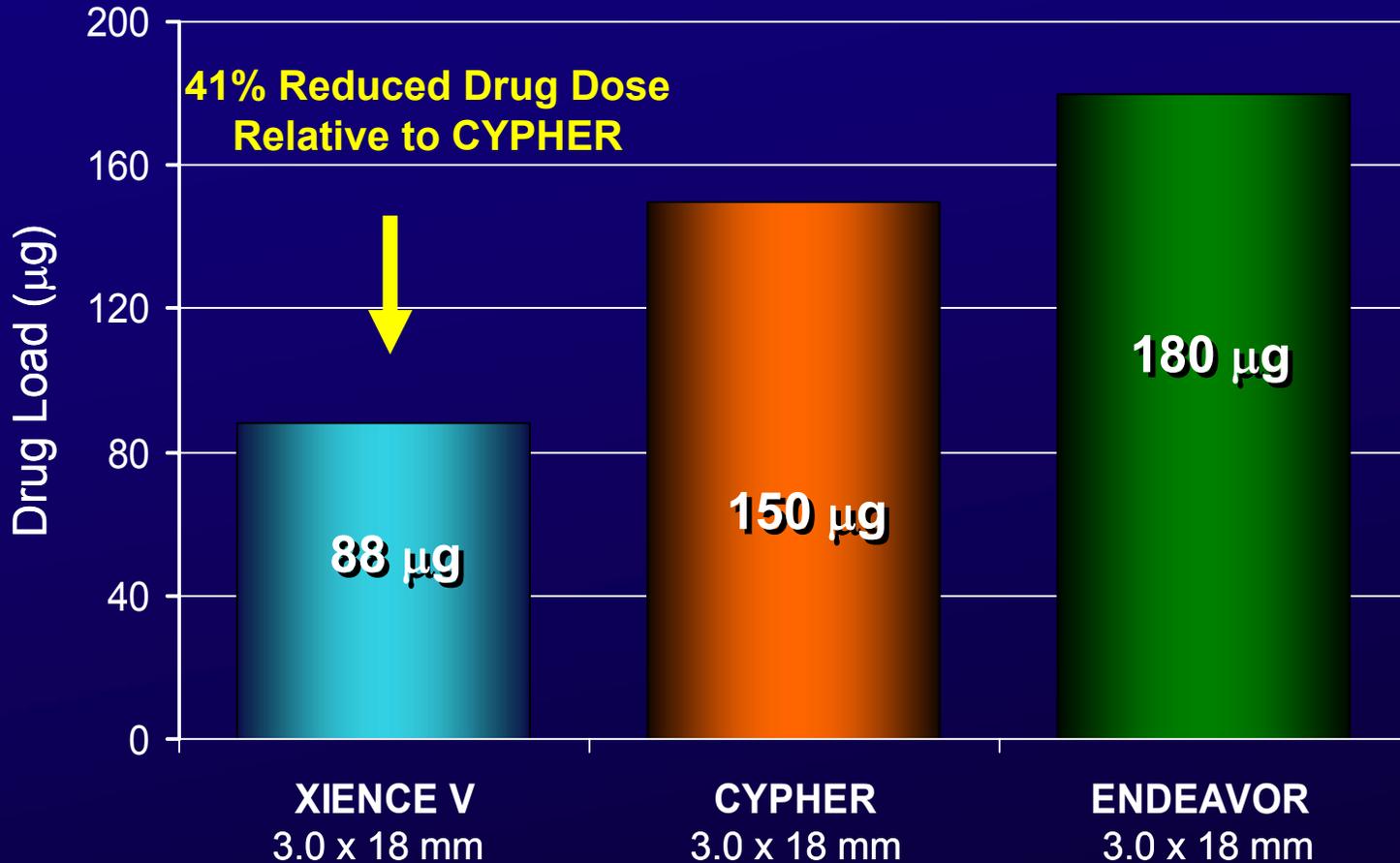
XIENCE V

Clinical Dose Selection

- Studied wide range of drug doses in porcine coronary arteries, from $100 \mu\text{g}/\text{cm}^2$ to $800 \mu\text{g}/\text{cm}^2$
- Observed sufficient drug effect at $100 \mu\text{g}/\text{cm}^2$ with no evidence of toxicity or medial necrosis at $800 \mu\text{g}/\text{cm}^2$
- Lowest effective dose of $100 \mu\text{g}/\text{cm}^2$ selected for clinical development

XIENCE V

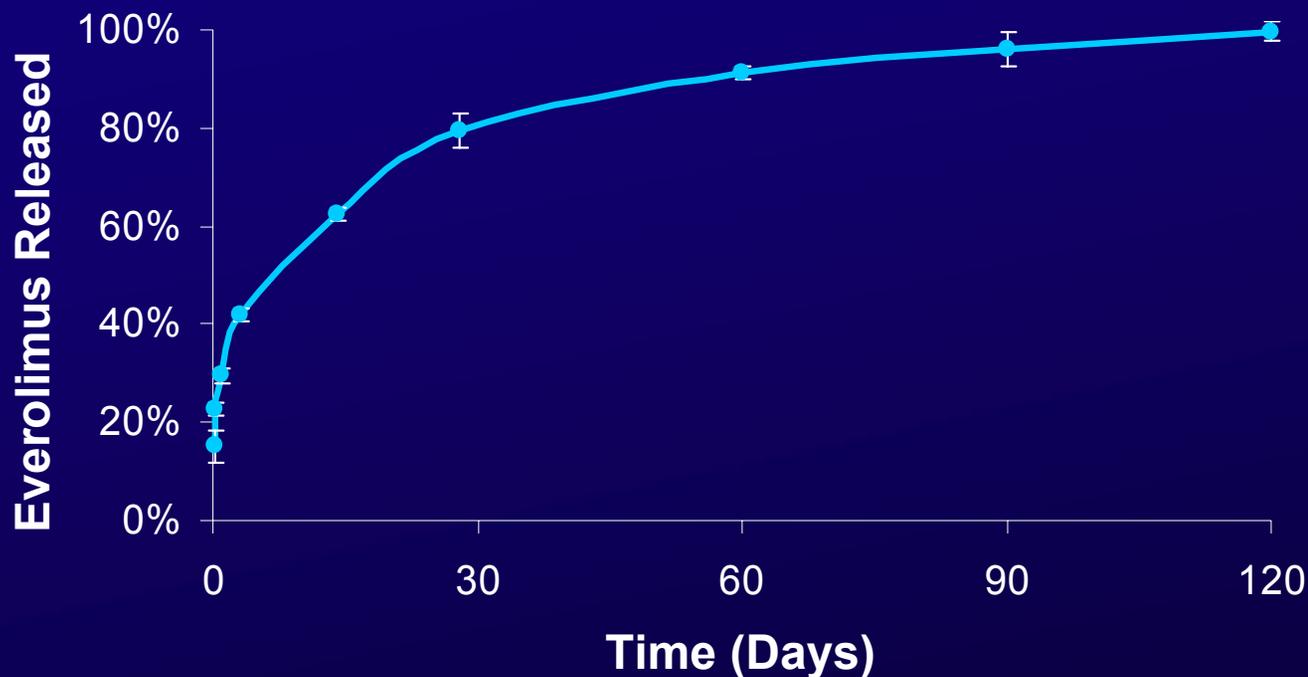
Reduced Drug Dose



Achieved effectiveness with reduced drug loading

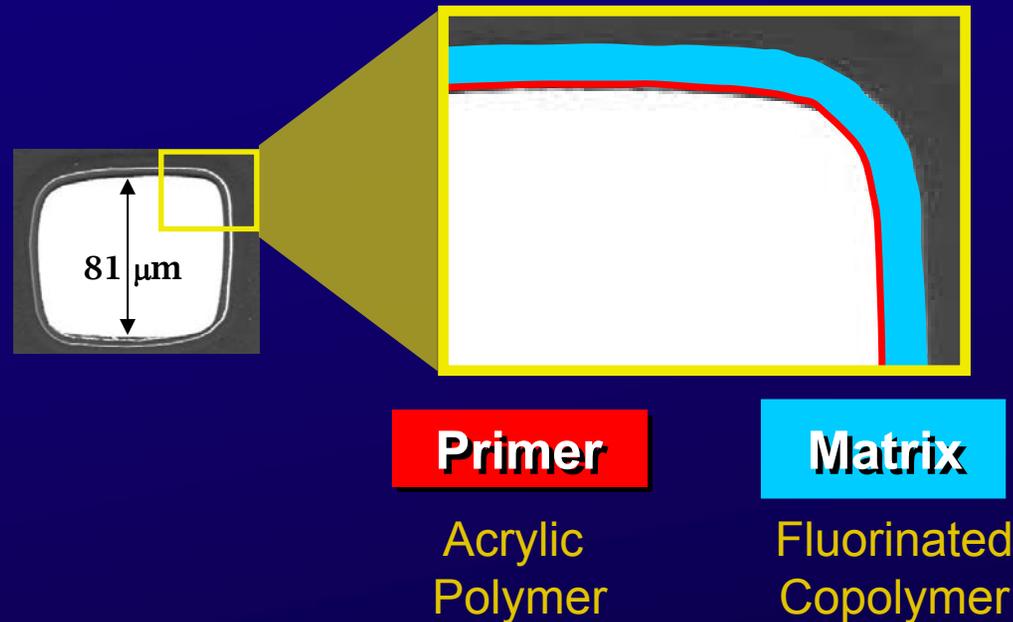
XIENCE V

Cumulative *in vivo* Drug Release (Porcine Model)



Consistent and well controlled drug elution *in vivo* with complete elution by 120 days

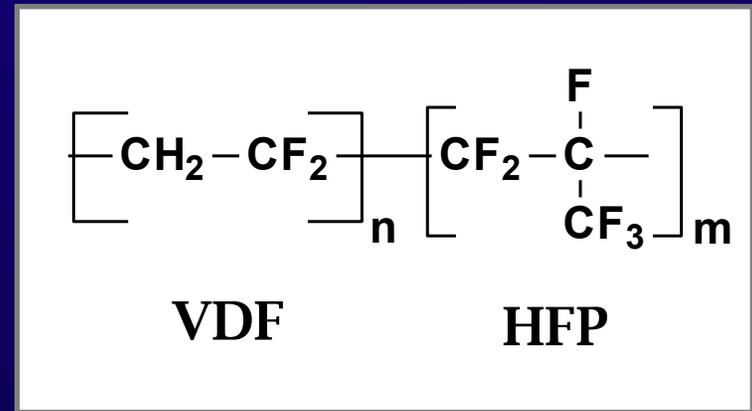
XIENCE V Coating Design



- Primer and Matrix system enables design optimization for excellent coating integrity and drug release control
- Selection of fluorinated copolymer minimizes unwanted adhesion to delivery balloon

Drug Matrix Fluorinated Copolymer

- Ultra-pure copolymer composed of VDF and HFP monomers
- Used in cardiovascular, neurological and ophthalmic sutures
- VDF-HFP ratio allows for optimization of coating **elasticity** and **toughness**
- Durable C-C backbone and covalent C-F bonds provide outstanding degree of **stability** and **biocompatibility**
- Stable molecular weight and mass *in vivo*
- **Excellent hemocompatibility**



VDF = vinylidene fluoride

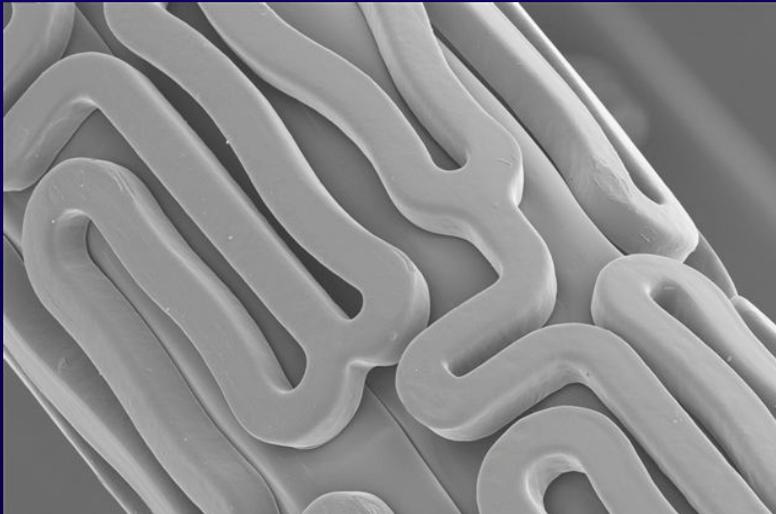
HFP = hexafluoropropylene

XIENCE V

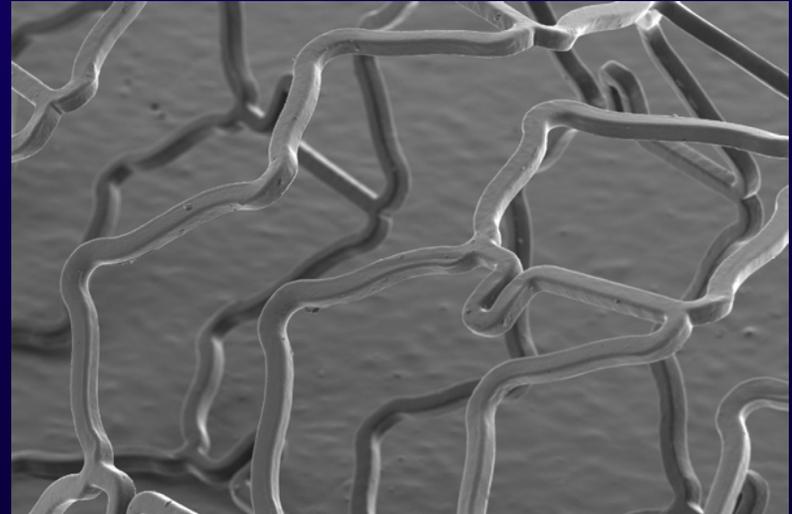
Coating Integrity

- Coating designed to minimize webbing, bridging, and strut-strut contact in crimped state
- Coating integrity maintained after simulated use, stent expansion and fatigue testing

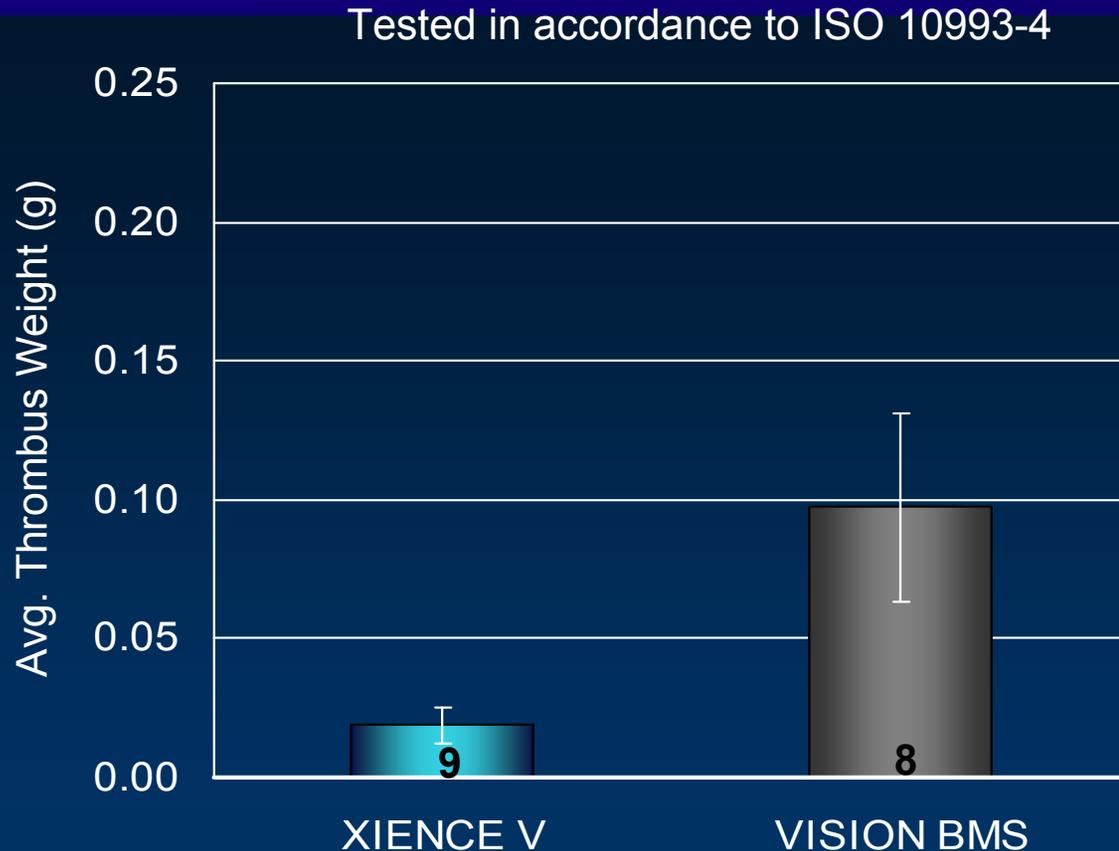
Crimped



Post-expansion



XIENCE V Hemocompatibility Unheparinized *ex vivo* Shunt Study



Study performed by Dr. Stuart K. Williams, Department of Biomedical Engineering, University of Arizona

XIENCE V Polymer Compatibility (Porcine Model)

VISION BMS



XIENCE V Fluorinated Copolymer



Polymer response equivalent to VISION BMS

XIENCE V

Design Summary

- Built on proven VISION Stent and Stent Delivery System
 - ✓ Flexible stent with thin struts
 - ✓ Proven deliverability
- Developed thin, biocompatible drug coating
 - ✓ Effective with low drug loading
 - ✓ Stable polymer
 - ✓ Uniform, conformal coating
 - ✓ Controlled and complete release of drug
 - ✓ Hemocompatibility and vascular compatibility

Pre-Clinical Program Overview

Leslie Coleman, DVM, MS, DACLAM
Director, Preclinical Research
Abbott Vascular

XIENCE V

Pre-Clinical Program Overview

- Biocompatibility
- Pharmacokinetics
- Comprehensive safety assessment
- Endothelial coverage & function

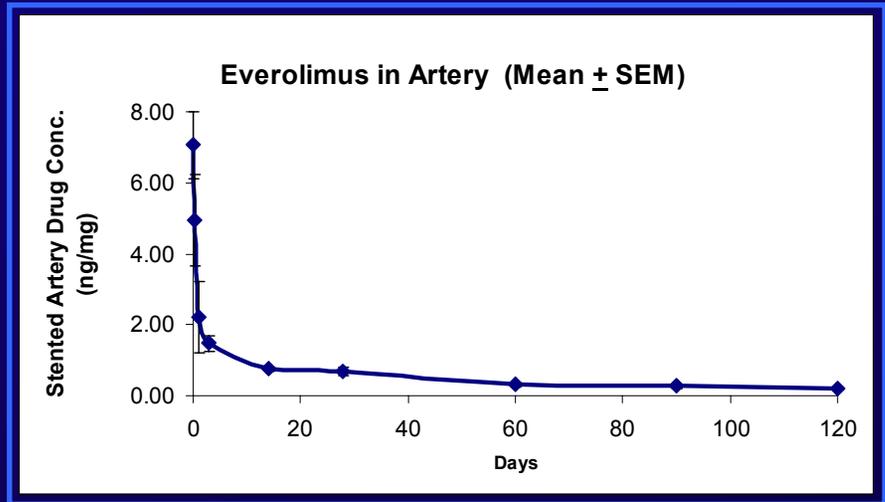
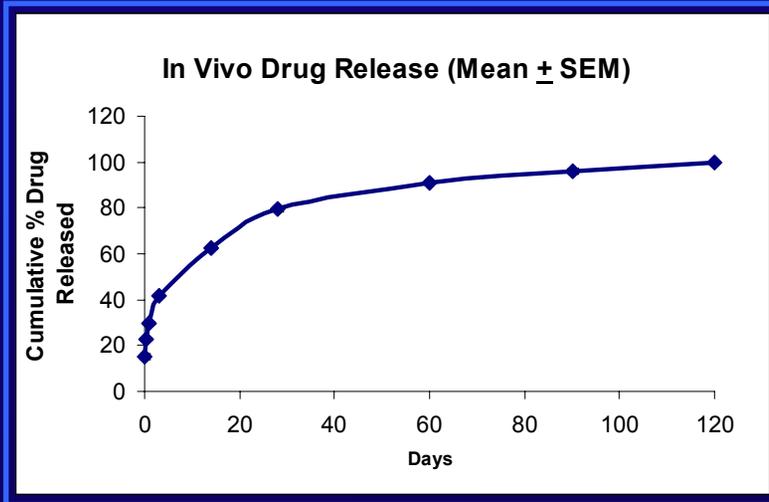
XIENCE V

Biocompatibility Evaluation

TEST	Samples Tested			
	XIENCE V	2.6X XIENCE V	Polymer Only	Results
Cytotoxicity (<i>in vitro</i> , MEM elution)	✓	✓	✓	Pass
Sensitization (Guinea Pig)	✓	✓	✓	Pass
Intracutaneous Reactivity (Rabbit)	✓	✓	✓	Pass
Systemic Toxicity, Acute (Mouse)	✓	✓	✓	Pass
Pyrogenicity/BET (LAL)	✓	✓	NA	Pass
Pyrogenicity (Rabbit)	✓	✓	NA	Pass
Hemolysis (<i>in vitro</i>)	✓	✓	NA	Pass
Coagulation (PT, PTT)	✓	✓	NA	Pass
Subchronic Toxicity: 90 day (Rabbit)	NA	✓	NA	Pass
Implantation: 7 day (Rabbit)	NA	NA	✓	Pass
Genotoxicity (<i>in vitro</i>)	NA	✓	NA	Pass
Teratology (SD Rat)	✓	NA	NA	Pass
Carcinogenicity (CB61F1-Tg rasH2 Mouse)	✓	NA	NA	Pass

SCIENCE V

Pre-Clinical Pharmacokinetics



Porcine model, 6 stents / time point

- Consistent controlled complete drug release
- Effective Arterial Delivery:
Controlled release of everolimus to target tissue

XIENCE V

Clinical Pharmacokinetics

PK Parameters	Oral Dose* (Novartis)	SPIRIT III RCT & 4.0 arm Registry (N=17)	SPIRIT III (Japan) (N=17)	SPIRIT II (OUS) (N=39)
Dosage Range	0.75 & 1.5 mg bid	53 – 181 µg	88 – 264 µg	53 – 588 µg
C_{max} Range (ng/mL)	11.1 ± 4.6 & 20.3 ± 8.0	0.17 - 2.40	0.29 - 2.11	0.14 -2.79
AUC_{0-last} Range (ng.hr/mL)	75 ± 31 & 131 ± 59	2.345 - 48.75	2.218 - 54.49	0.453 - 164.1

Results from all PK sub-studies were consistent and showed limited systemic exposure up to a total dose of 588 µg

* Therapeutic window following oral delivery 3-8 ng/mL

Systemic exposure to everolimus is below the minimum therapeutic blood level of 3 ng/mL

SCIENCE V

Comprehensive Safety Assessment

35 Animal Studies; 2 Species; 28 Days to 2 Years

Porcine Coronary Artery Model

- 28, 90, 180 days
- 1, 2 years

Rabbit Iliac Artery Model

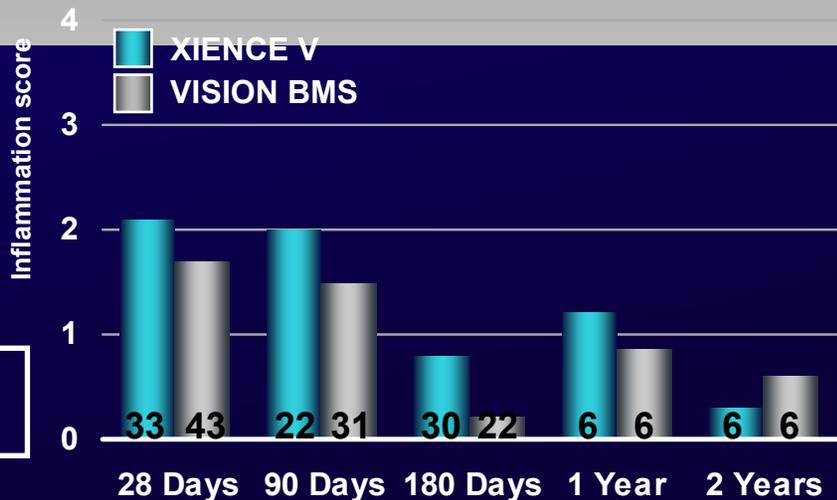
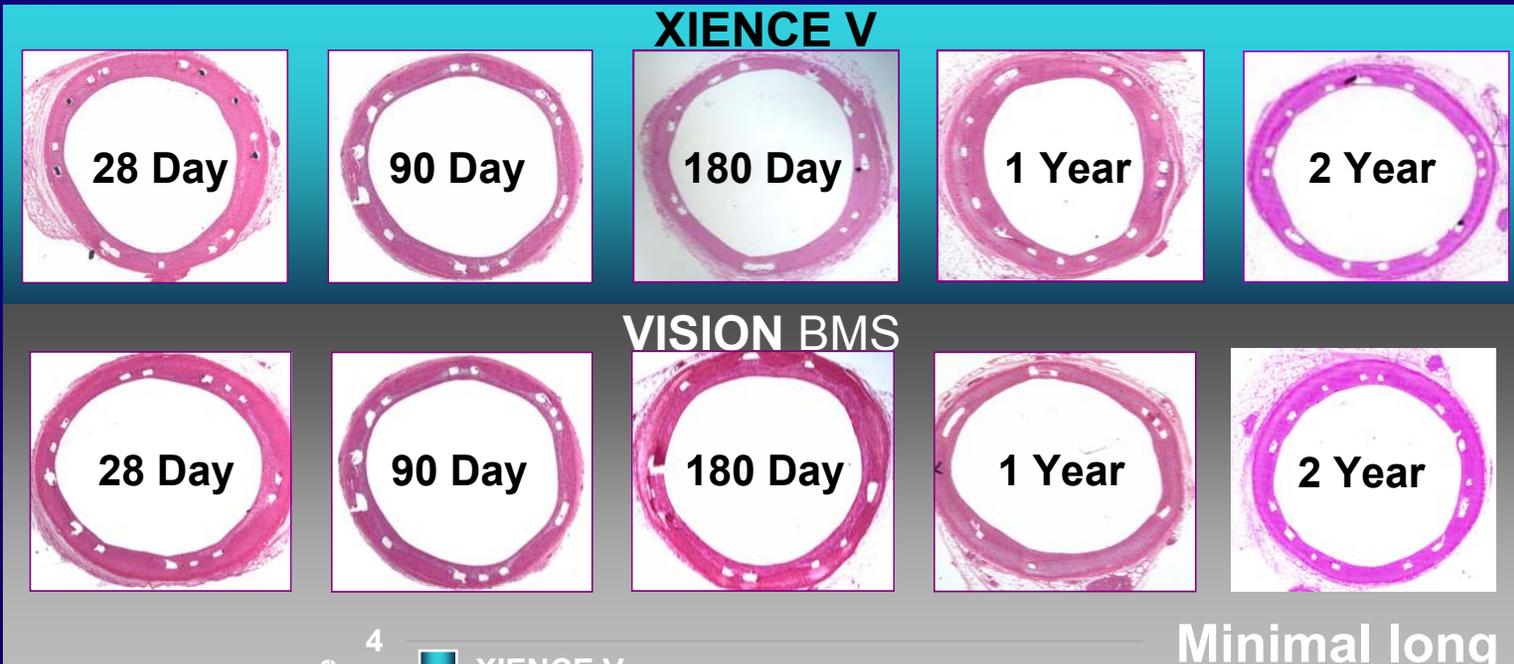
- 28, 90 days

		28 Day	90 Day	180 Day	1 Year	2 Year
Safety	Porcine Coronary Artery	✓	✓	✓	✓	✓
	Rabbit Iliac Artery	✓	✓			
Overlapping Safety	Porcine Coronary Artery	✓	✓	✓		
	Rabbit Iliac Artery	✓	✓			
Maximum Dose (8X) Safety	Porcine Coronary Artery	✓	✓	✓		
Polymer (1-3X) Safety	Porcine Coronary Artery	✓	✓	✓	✓	✓

Goal of DES Safety

- Effective drug delivery with rapid vessel healing
 - Smooth muscle cell rich neointima
 - Minimal persistent fibrin
 - Minimal long term inflammation
 - Rapidly endothelialized lumen

XIENCE V Porcine Safety Study 28 Days to 2 Years

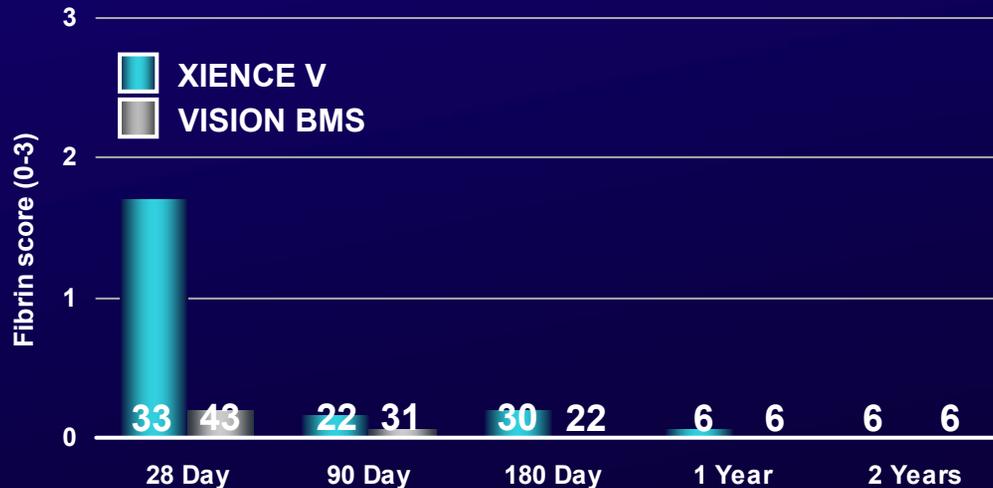


Inflammation score
0-1= background

Minimal long term
inflammation
consistent with
vessel healing

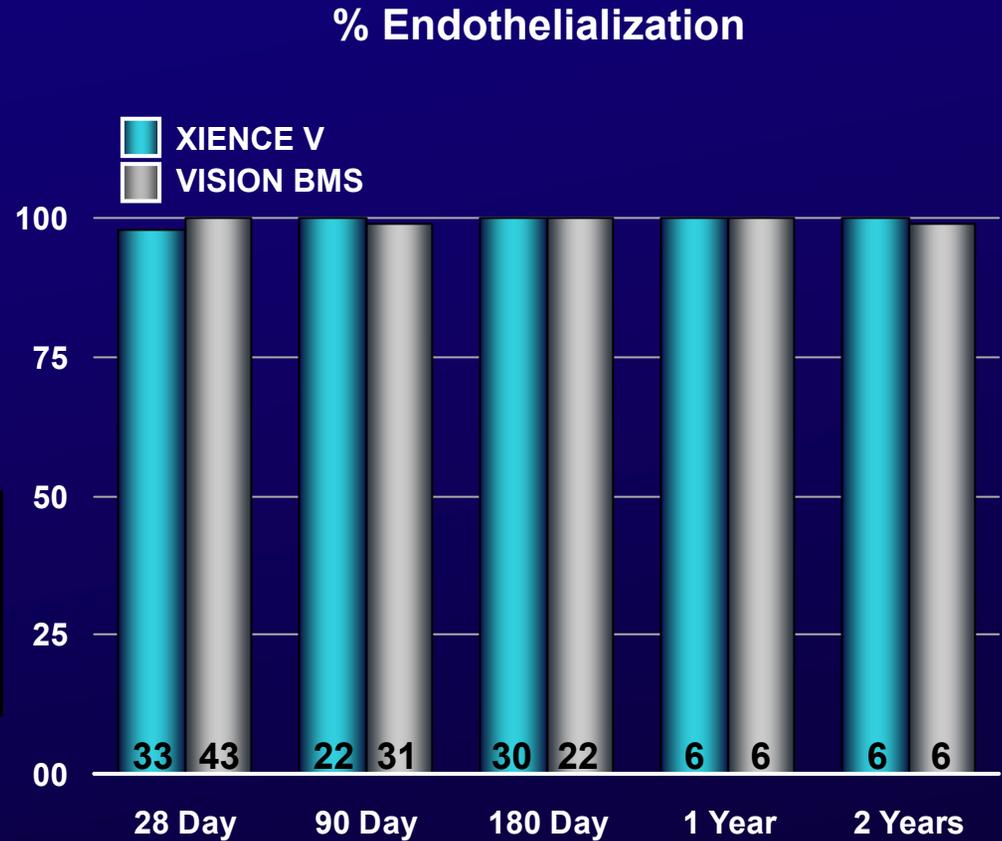
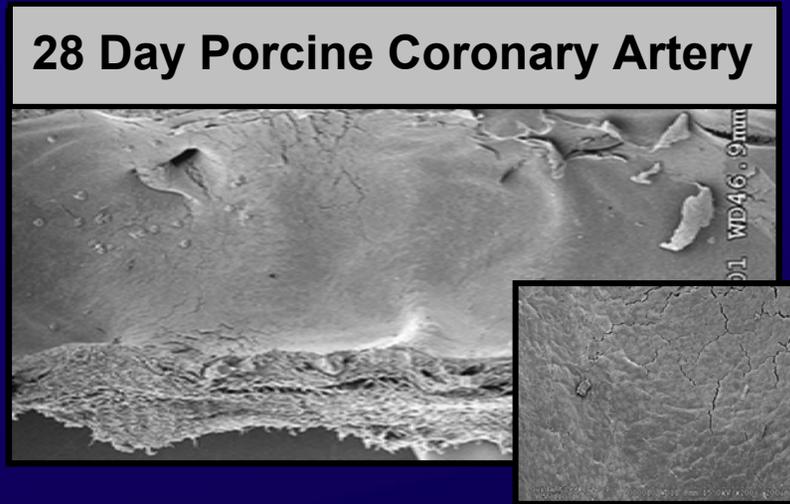
XIENCE V

Fibrin Resolution Post-Drug Elution



Resolution of fibrin consistent with vessel healing

XIENCE V Endothelialization



Luminal endothelialization complete by 28 days

SCIENCE V

Safety Response

Short term response

28, 90 days

Active Phase (drug elution)

- Fully endothelialized
- Neointimal coverage of struts
 - Peri-strut fibrin consistent with drug elution
 - Inflammation comparable to VISION BMS
 - No to minimal mineralization
 - No medial necrosis

Long term response

≥180 days

Post drug elution

- Fully endothelialized
- Quiescent healed vessel wall
 - Minimal to no peri-strut fibrin
 - Minimal inflammation comparable to VISION BMS
 - No to minimal mineralization
 - No medial necrosis

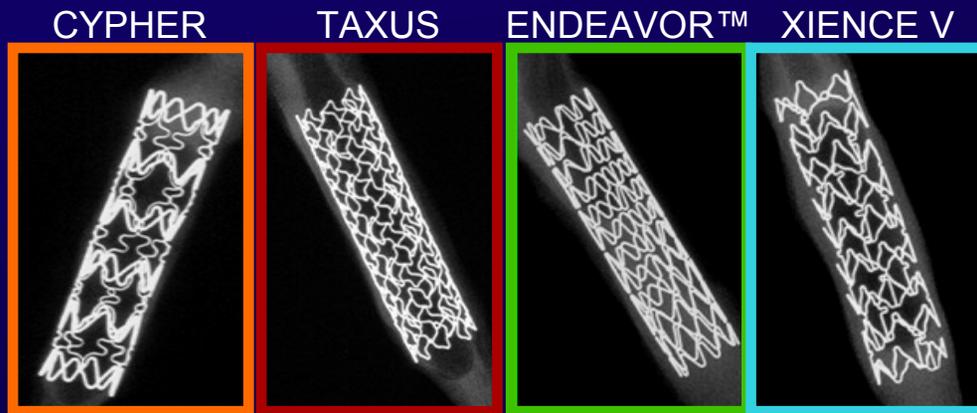
Safety consistent with vessel healing

XIENCE V Safety

- XIENCE V safety has been demonstrated in 2 animal models with data out to 2 years
- Goal of DES safety program has been met
 - ✓ Smooth muscle cell rich neointima
 - ✓ Minimal persistent fibrin
 - ✓ Minimal long term inflammation
 - ✓ Rapidly endothelialized lumen

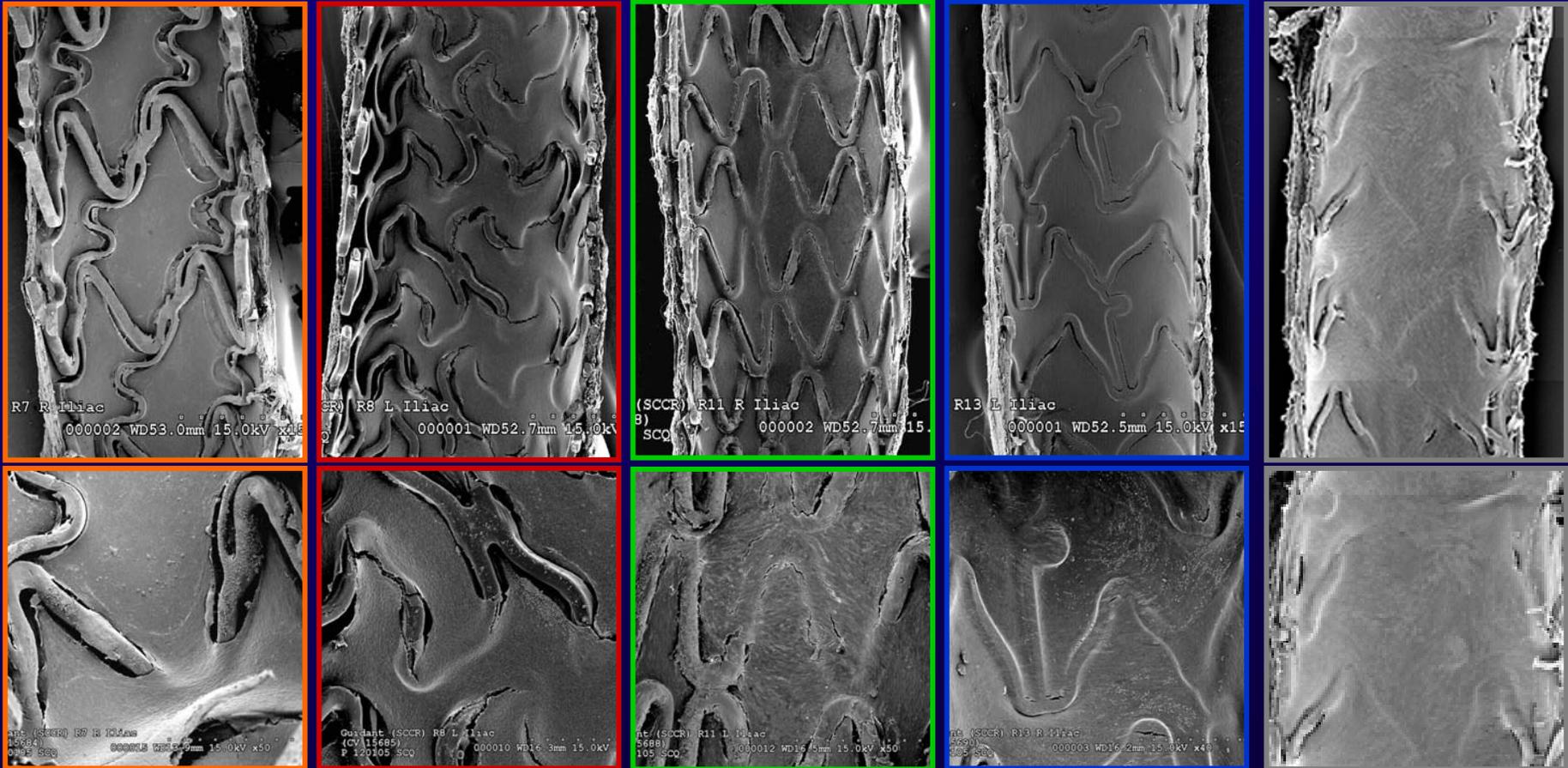
Comprehensive Endothelial Cell Coverage and Function Evaluation

- Qualitative and Quantitative Scanning Electron Microscopy evaluation of endothelial cell coverage
- Confocal microscopy evaluation of specific endothelial markers
- Molecular quantification of specific endothelial markers



Comparison of Endothelialization following Implantation of CYPHER, TAXUS, ENDEAVOR and XIENCE V Stents in Rabbit Iliac Arteries

Qualitative Assessment of Endothelial Cell Coverage: 14-day Rabbit Iliac



CYPHER

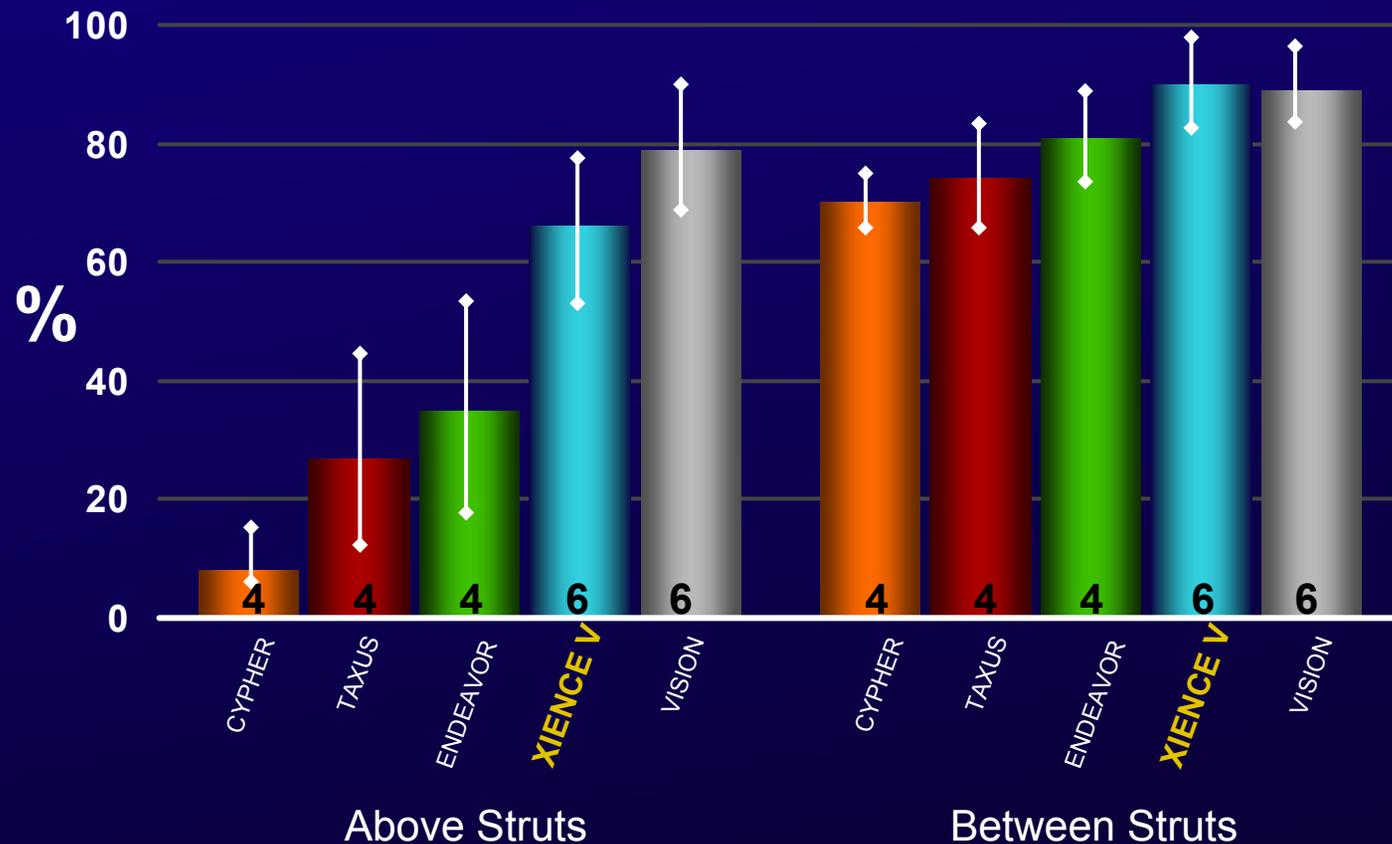
TAXUS

ENDEAVOR

XIENCE V

VISION

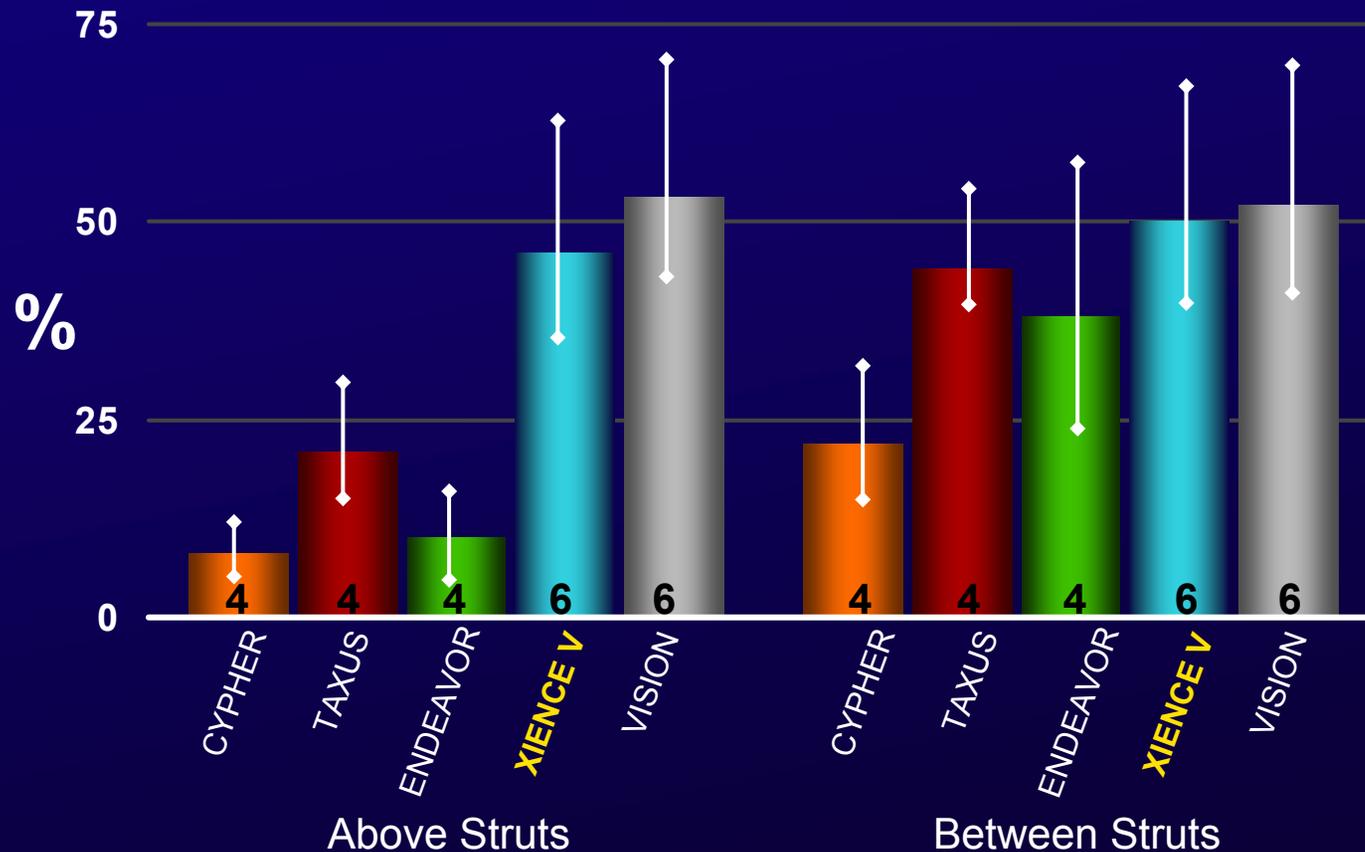
Quantitative Assessment of Luminal Endothelialization by SEM



Endothelial Cell Integrity and Functionality Assessed

- Platelet endothelial adhesion molecule (PECAM-1)
 - A membrane glycoprotein that is constitutively expressed by endothelial cells at cell borders, platelets and other cells; inhibits aggregation of platelets
- Vascular endothelial growth factor (VEGF)
 - Endothelial cell specific mitogen, and regulator of vascular permeability; upregulated in absence of confluent endothelial growth and down regulated with complete endothelialization

PECAM-1 Expression: XIENCE V Consistent with Endothelialization

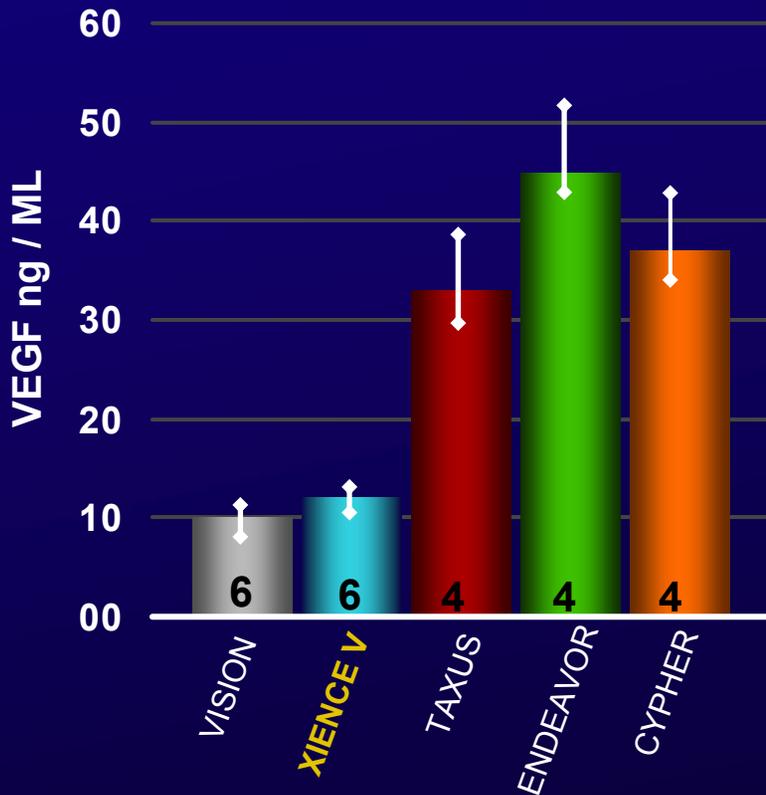


Error bar = ± 1 SE

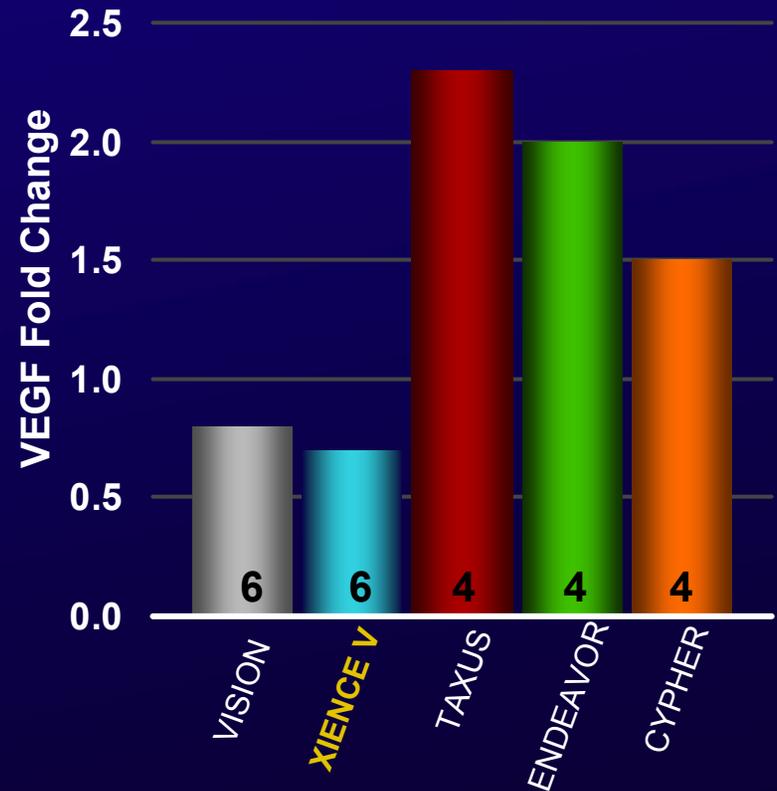
14 Days Rabbit Iliac

VEGF Production: VISION and XIENCE V Levels Consistent with Endothelialization

Protein Levels (ELISA)



Gene Expression (RT-PCR)



14 days Rabbit Iliac

XIENCE V

Endothelial Cell Coverage & Function

- XIENCE V demonstrates rapid re-endothelialization compared to other DES
- XIENCE V demonstrates enhanced endothelial cell function compared to other DES

Rapid endothelial cell coverage and function is consistent with vessel healing

SPIRIT Clinical Program

Gregg W. Stone, MD

Professor of Medicine, Columbia University Medical Center

Chairman, The Cardiovascular Research Foundation

Disclosure Slide

- Gregg W. Stone, MD
- Research support from Abbott Vascular and Boston Scientific

Integrated Pre-Approval and Post-Approval Clinical Program (N > 16,000)

Pre-approval Clinical Data

SPIRIT First

RCT 1:1 XIENCE V vs. VISION (n = 60) OUS

SPIRIT II

RCT 3:1 XIENCE V vs. TAXUS (n = 300) OUS

SPIRIT III

RCT 2:1 XIENCE V vs. TAXUS (n = 1,002) US

SPIRIT III 4.0

Registry 4.0 mm (n = 80) US

Ongoing and Planned Clinical Data

SPIRIT III Japan

Registry (n = 88) Japan

SPIRIT IV

RCT XIENCE V vs. TAXUS[®] 2:1 Continued Access (n = 3,690) US

SPIRIT V

Registry (n = 2,700), RCT Diabetics 2:1 vs. TAXUS (n = 300) OUS

**XIENCE V
SPIRIT Women**

Registry (n = 1,550) RCT 2:1 vs. CYPHER[®] (n = 450) OUS

XIENCE V USA

Post-approval Registry – real world (n ~ 5,000) US

XIENCE India

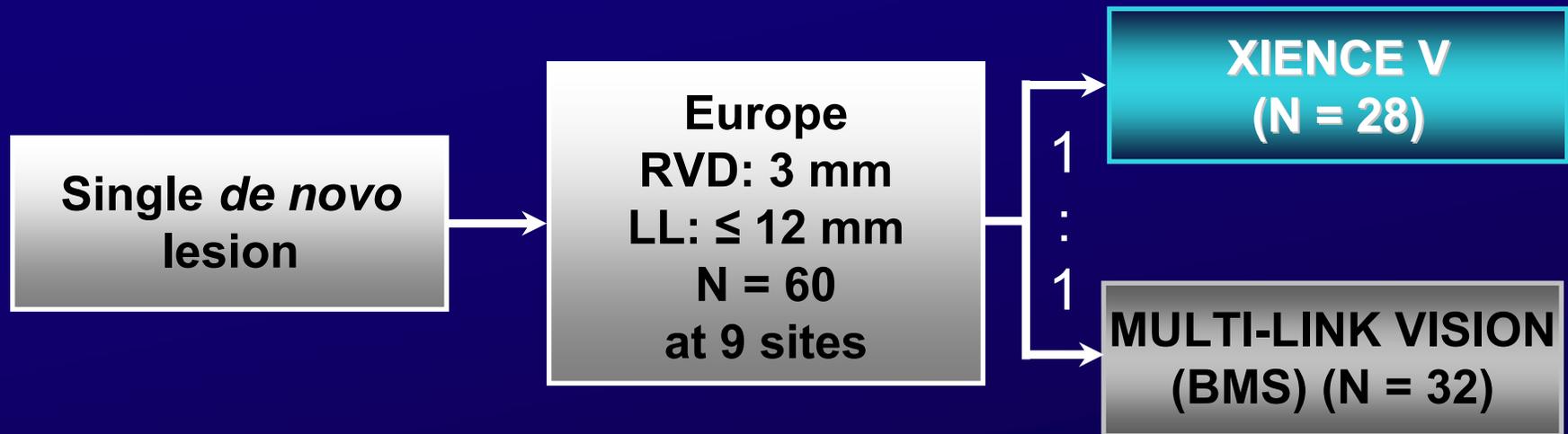
Post-approval Registry – real world (n ~ 1,000) OUS

**XIENCE V vs. VISION
DES vs. BMS**

SPIRIT FIRST

Randomized Controlled Trial

SPIRIT FIRST: Study Design (DES vs. BMS)

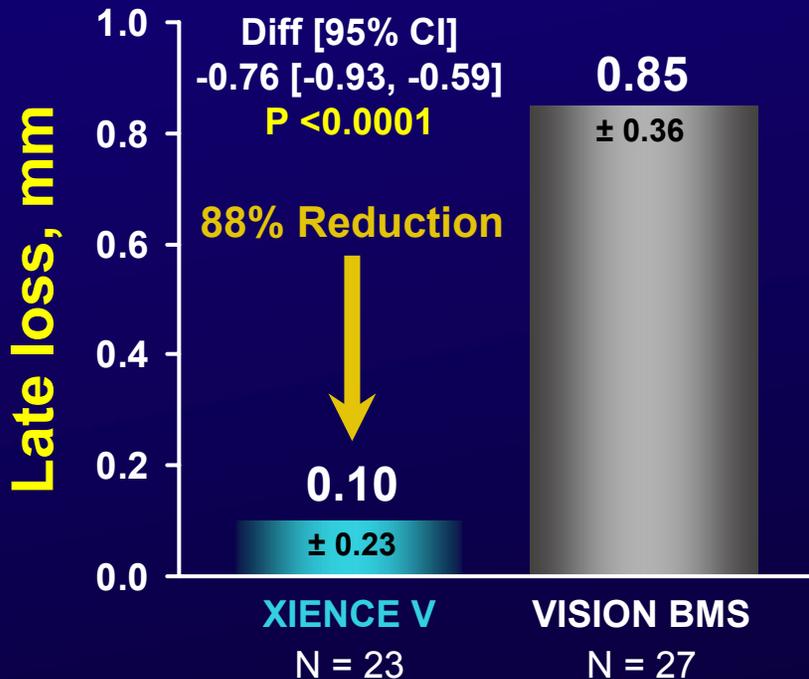


- Prospective, single blind, randomized trial in 60 pts
- Angiographic and IVUS follow-up at 180 days and one year
- Clinical follow-up up to 5 yrs
- Primary endpoint: Angiographic in-stent late loss (LL) at 180 days
- Major secondary endpoint: IVUS volume obstruction (% VO) at 180 days
- Both endpoints powered for superiority
- PI: Patrick W. Serruys, MD

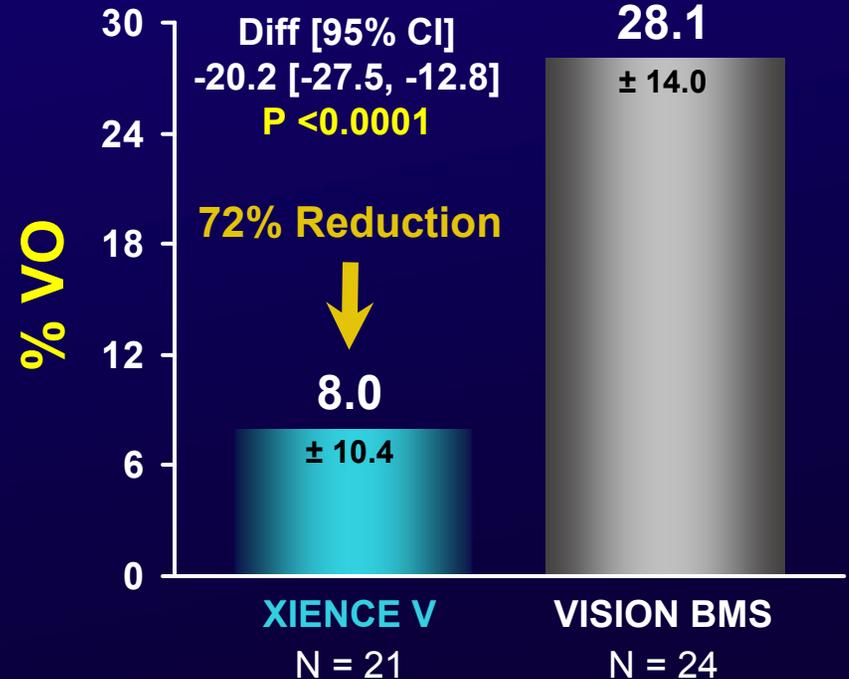
SPIRIT FIRST: 6 Month Results In-Stent LL and % VO

DES vs. BMS

Primary Endpoint In-stent Late Loss



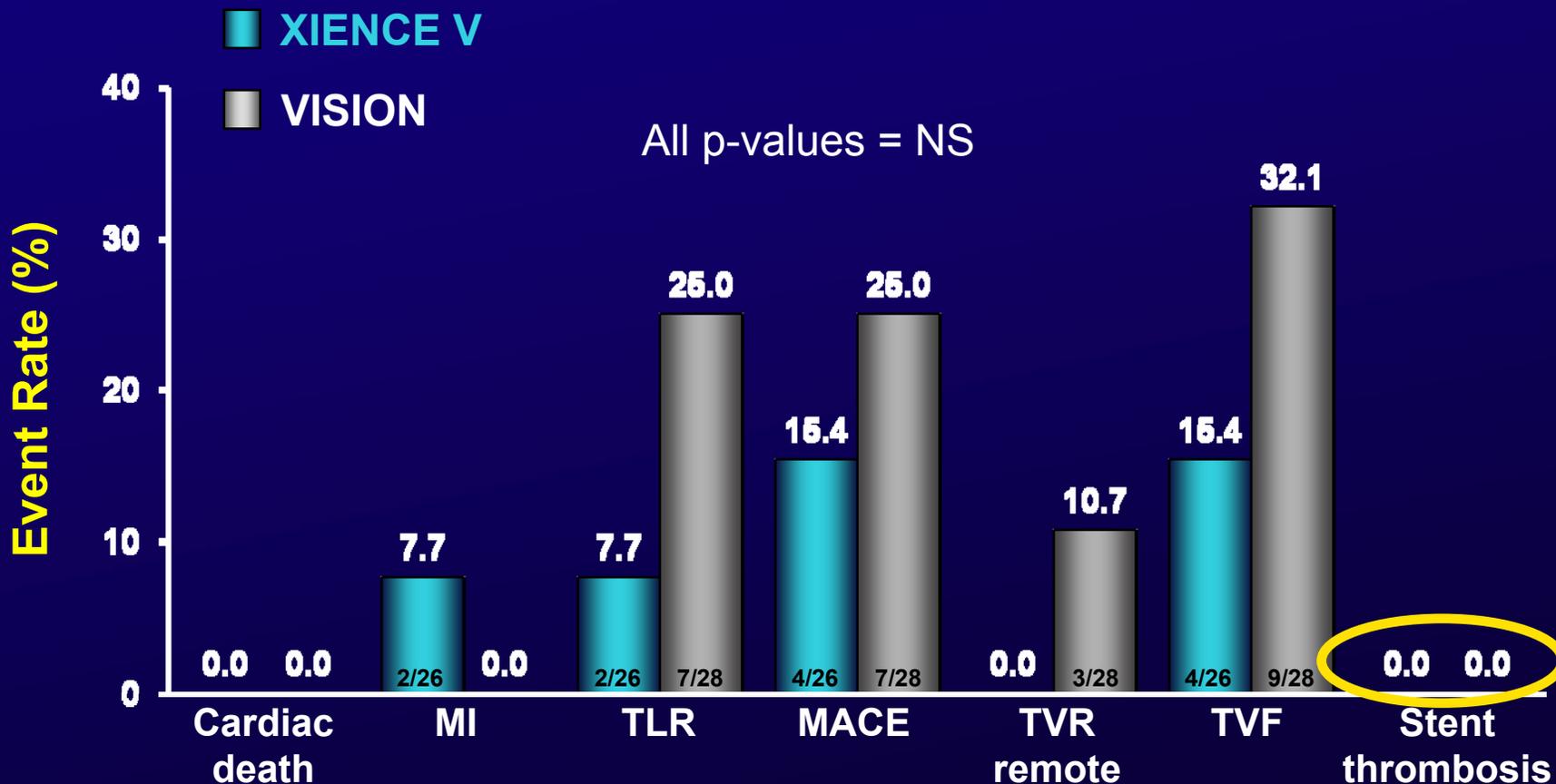
Major Secondary Endpoint IVUS % Volume Obstruction (%VO)



SPIRIT FIRST: 3 Year Results

Event Rates

DES vs. BMS



MACE = Cardiac death, MI, or ischemic TLR
TVF = Cardiac death, MI, or ischemic TVR

Conclusions

SPIRIT FIRST

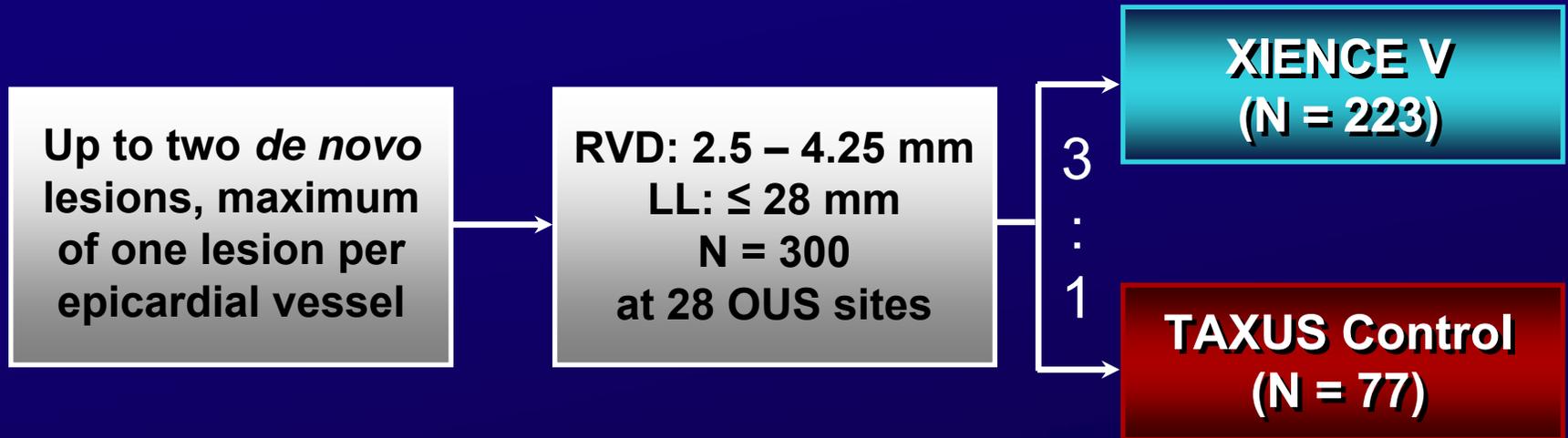
The SPIRIT FIRST Trial **met both its pre-specified primary and major secondary endpoints**, demonstrating **superiority** of the XIENCE V stent compared to the bare metal ML VISION stent in reducing late loss and % volume obstruction

**XIENCE V vs. TAXUS
DES vs. DES**

SPIRIT II

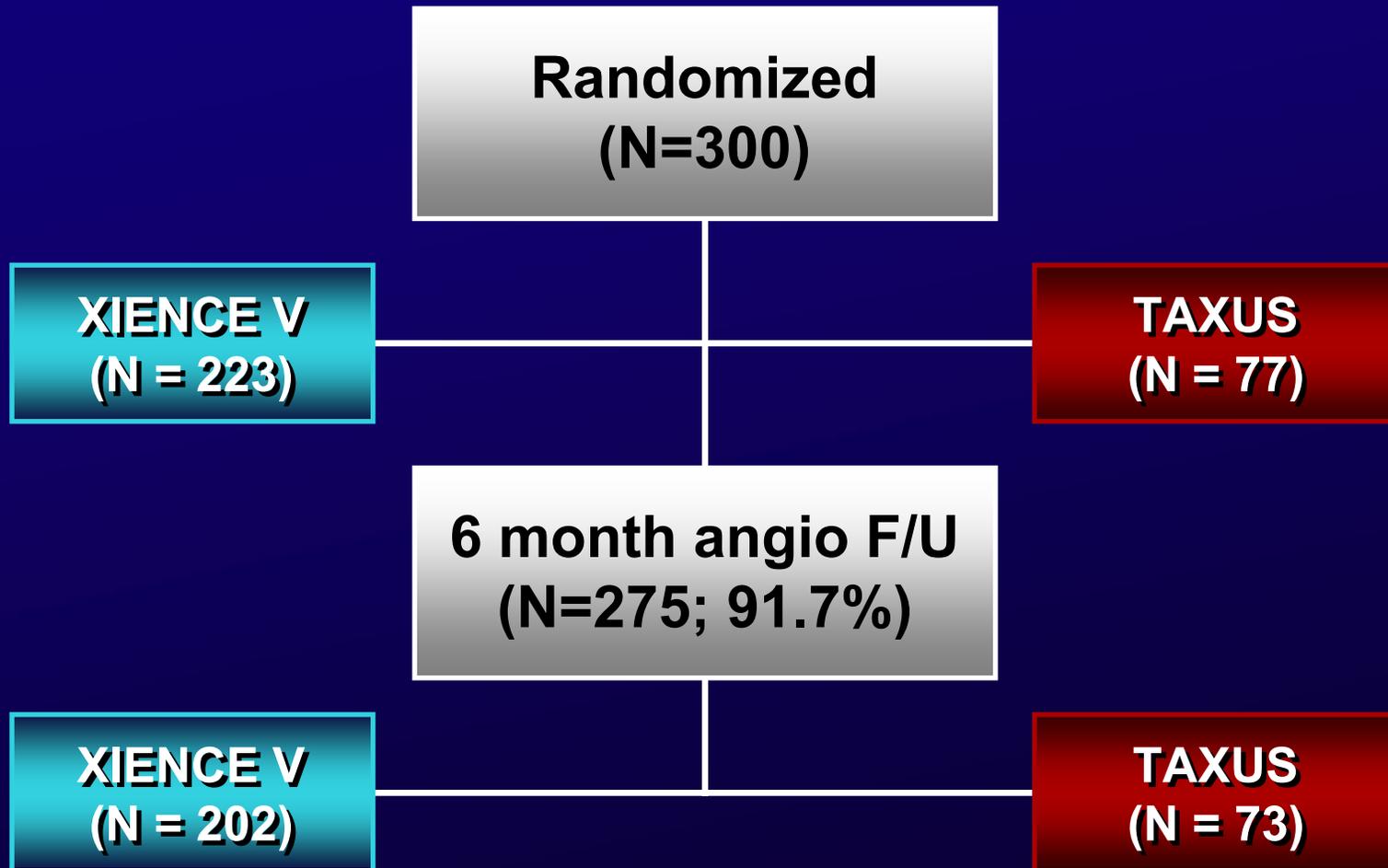
Randomized Controlled Trial

SPIRIT II: Study Design (DES vs. DES)



- Prospective, single blind, randomized trial in 300 pts
- Angiographic and IVUS follow-up: 180 days (all pts), and 2 years (152 pts)
- Clinical follow-up up to 5 years
- Primary endpoint: Angiographic in-stent late loss at 180 days (powered for sequential non-inferiority and superiority)
- Powered secondary endpoint: Angiographic in-segment late loss at 180 days (powered for non-inferiority)
- PI: Patrick W. Serruys, MD

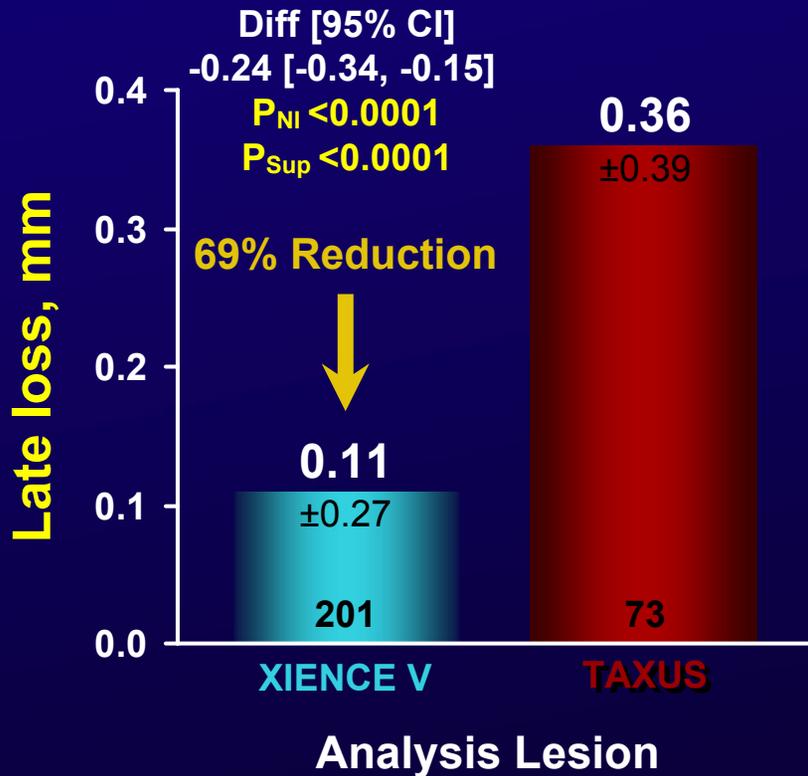
SPIRIT II: Angiographic Patient Flow at 6 Months



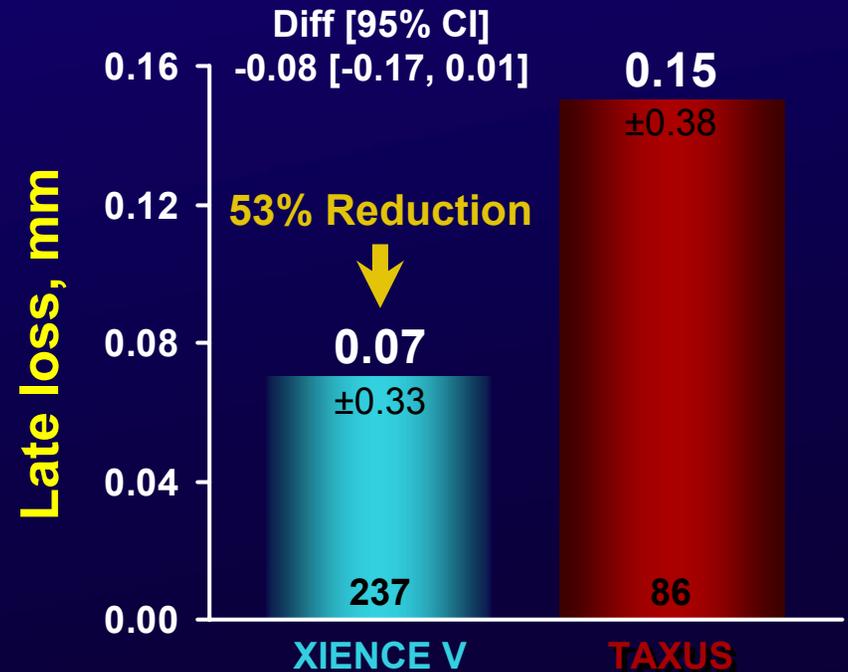
SPIRIT II: 6 Months Results In-Stent and In-segment LL

DES vs. DES

Primary Endpoint In-stent Late Loss



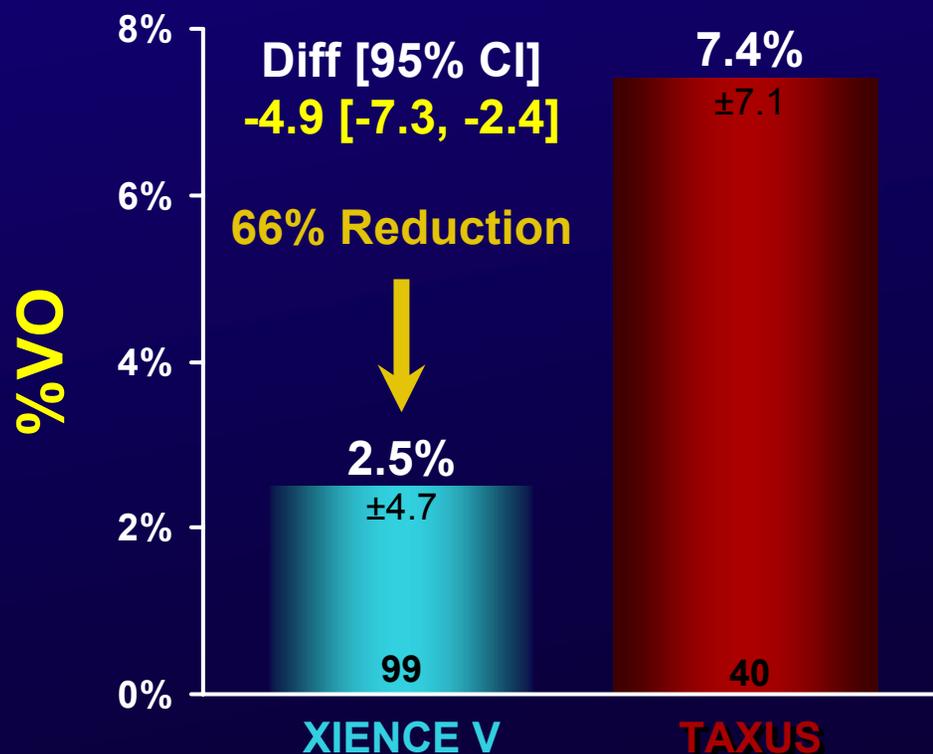
Secondary Endpoint In-segment Late Loss



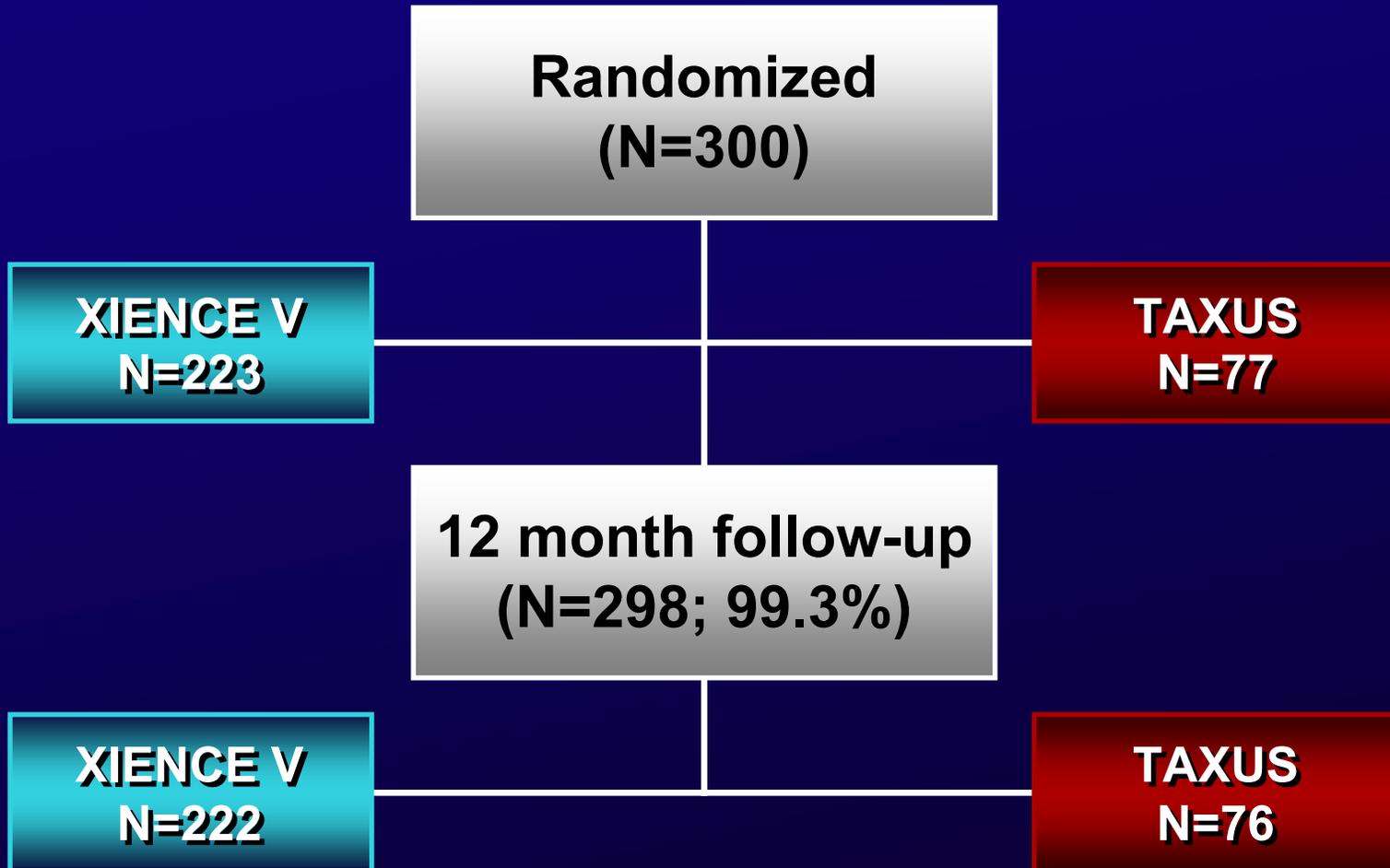
SPIRIT II: 6 Months Results

IVUS % Volume Obstruction

DES vs. DES
IVUS Percent
% Volume Obstruction

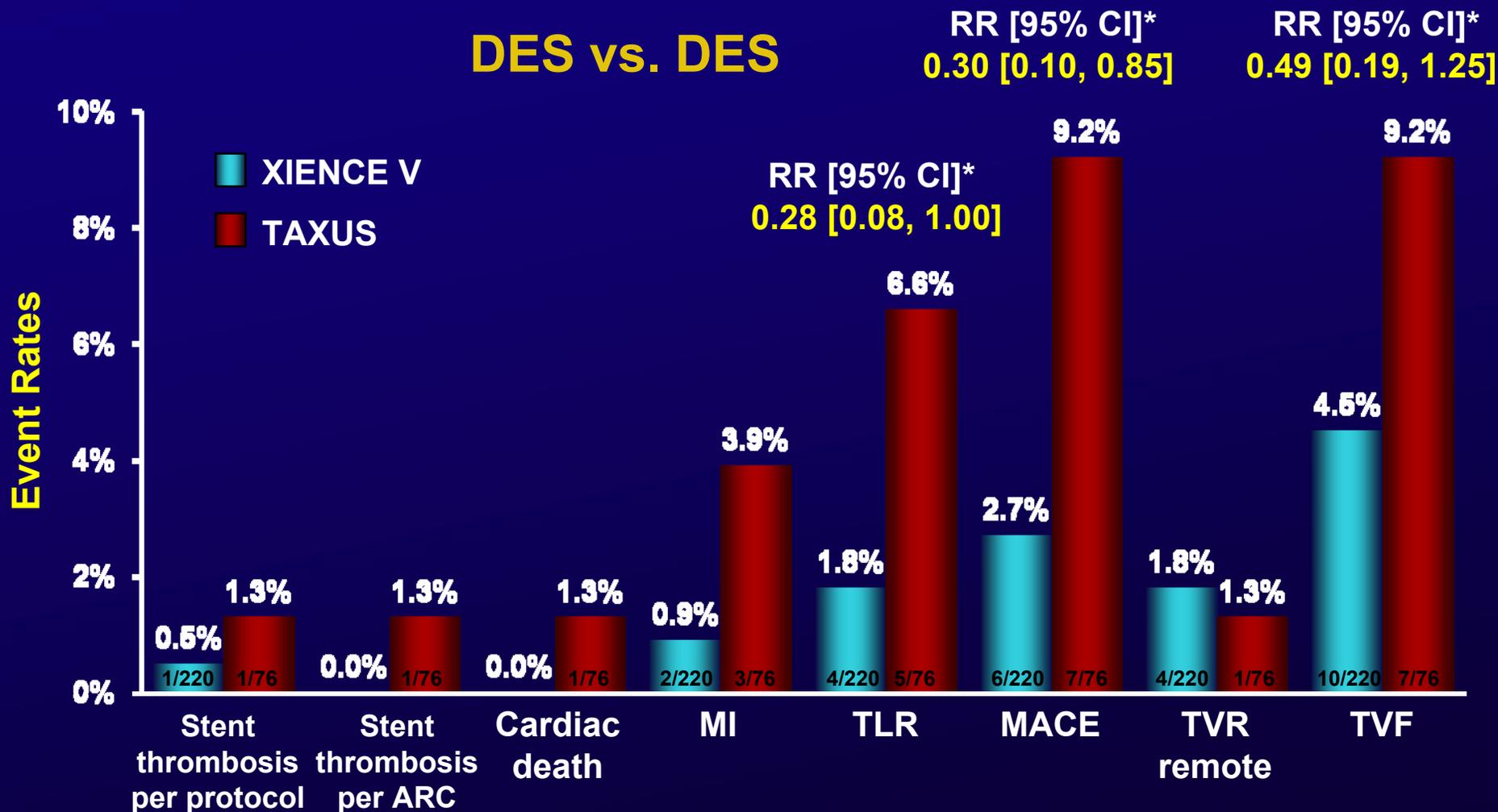


SPIRIT II: Clinical Follow-up Patient Flow at One Year



SPIRIT II: One Year Results

Event Rates



MACE = Cardiac death, MI, or ischemic TLR
TVF = Cardiac death, MI, or ischemic TVR

* Confidence Intervals are for descriptive purposes only and not adjusted for multiple comparisons

Conclusions

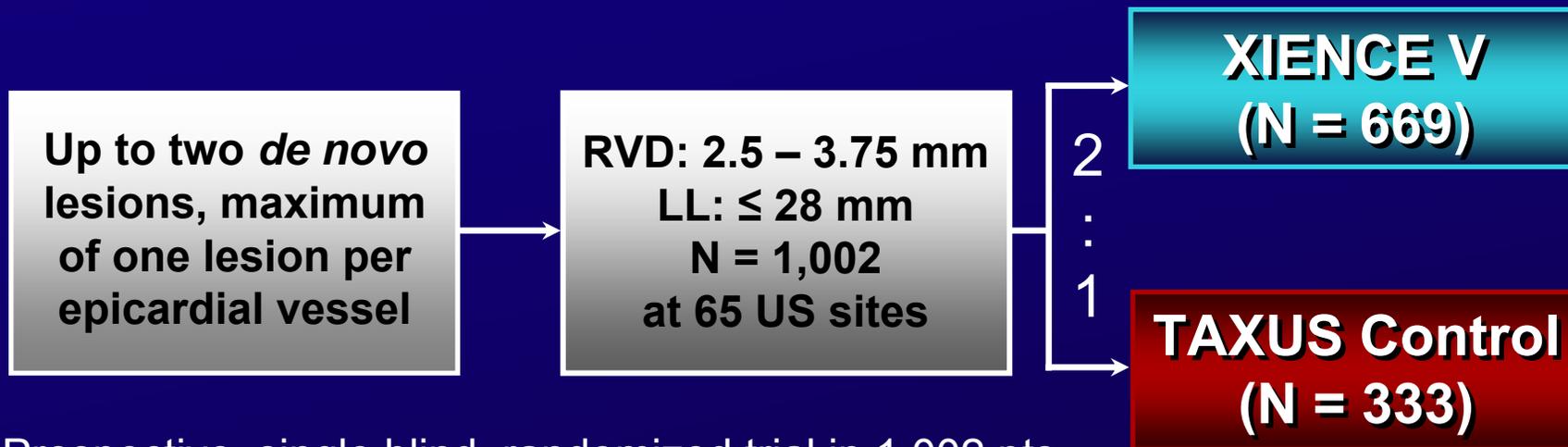
SPIRIT II

The SPIRIT II Trial **met its pre-specified primary endpoint**, demonstrating **superiority** of the XIENCE V stent compared to the TAXUS stent in reducing in-stent angiographic late loss

XIENCE V vs. TAXUS DES vs. DES

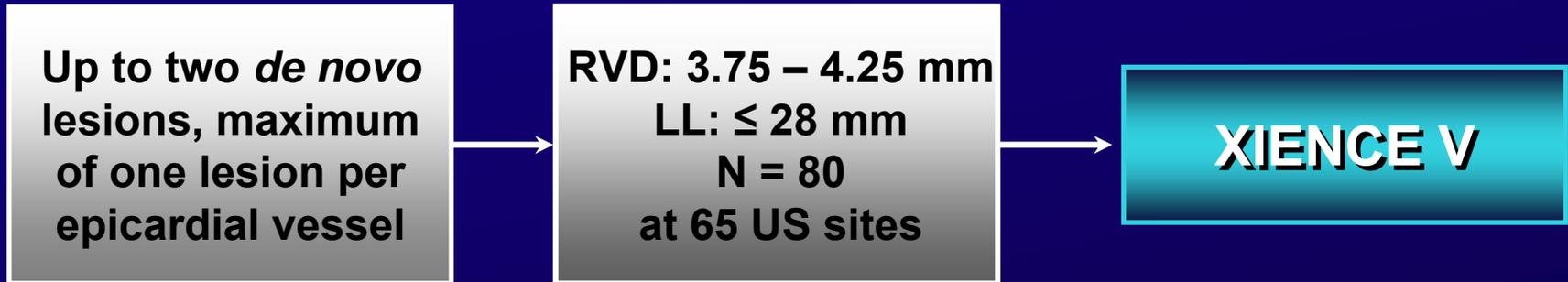
**Pivotal U.S. SPIRIT III
Randomized Controlled Trial**

SPIRIT III: RCT (DES vs. DES)



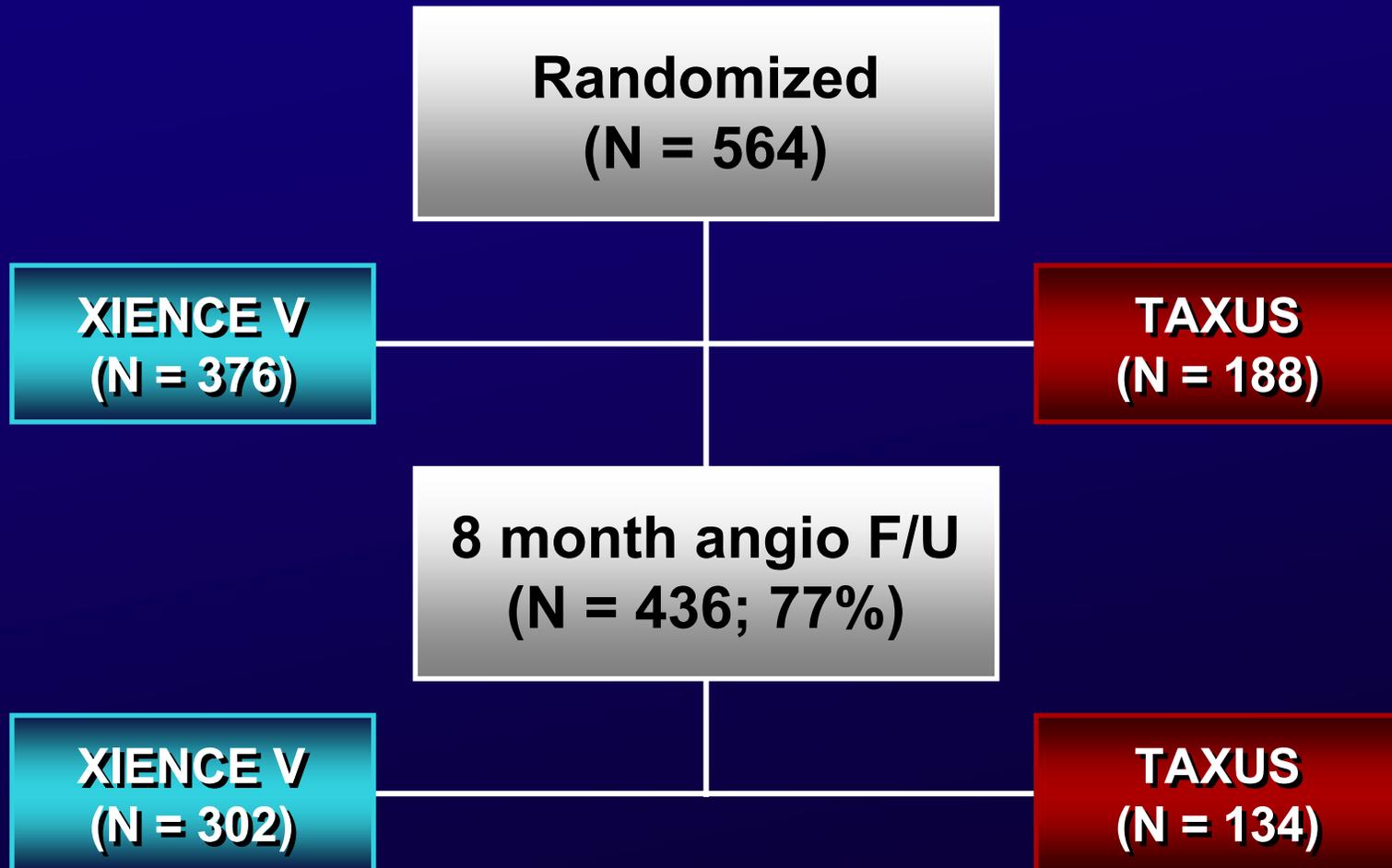
- Prospective, single blind, randomized trial in 1,002 pts
- Angiographic and IVUS follow-up at 8 months in pre-specified subsets
- Clinical follow-up up to 5 years in all patients
- Primary endpoint: Angiographic in-segment late loss at 8 months (powered for non-inferiority and superiority) (N = consecutive 564 patients)
- Major secondary (co-primary) endpoint : Ischemia-driven target vessel failure (TVF) at 9 months (cardiac death, MI, TVR) (powered for non-inferiority)
- Both endpoints required to be met for regulatory approval
- PI: Gregg W. Stone, MD

SPIRIT III: 4.0 mm Stent Registry



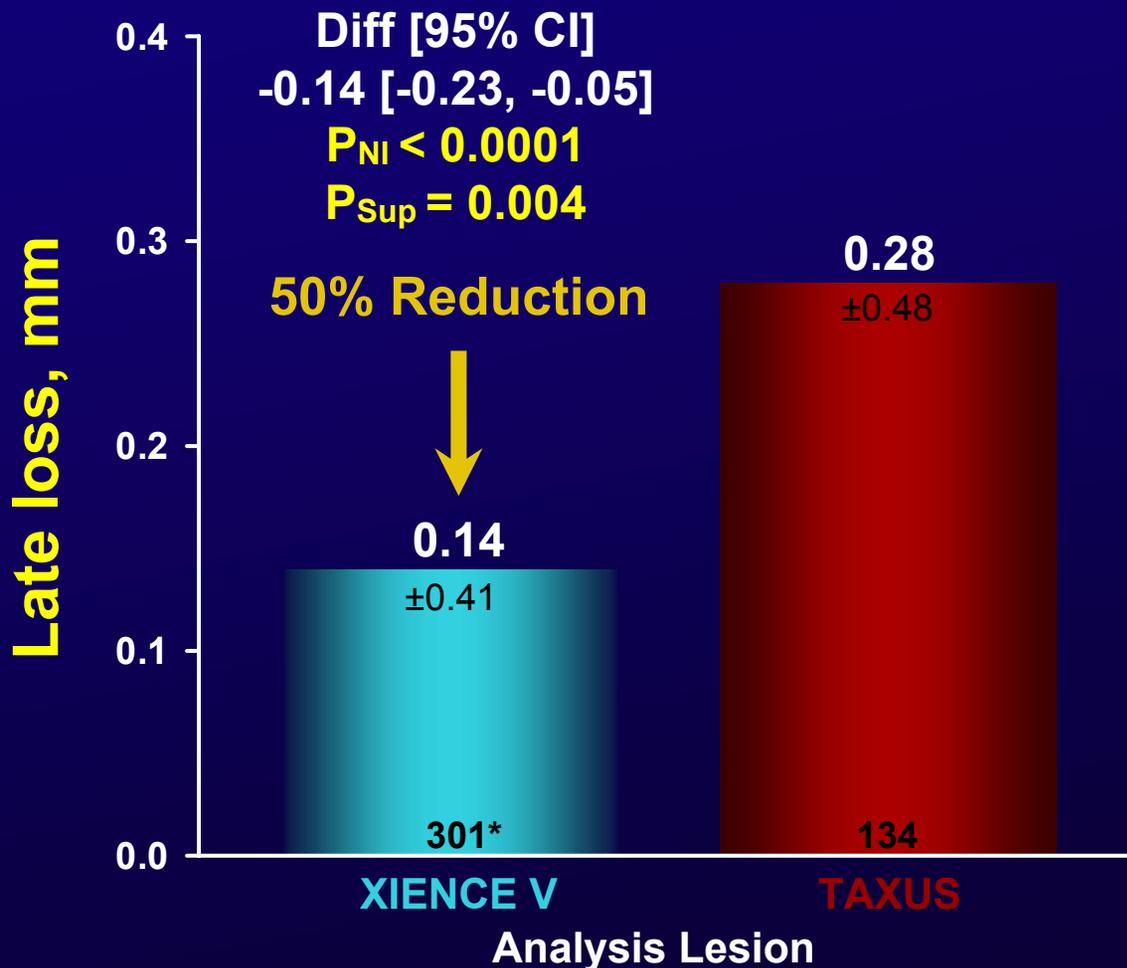
- Prospective, single blind, 4.0 mm registry (RVD 3.75 - 4.25 mm) compared to concurrent TAXUS control from Spirit III, with angiographic follow-up at 8 months and clinical follow-up up to 5 years in all patients
- Primary endpoint for regulatory approval: Angiographic in-segment late loss at 8 months (powered for non-inferiority compared to TAXUS from Spirit III)

SPIRIT III: Angiographic Patient Flow at 8 Months



SPIRIT III: Primary Endpoint In-segment LL at 8 Months

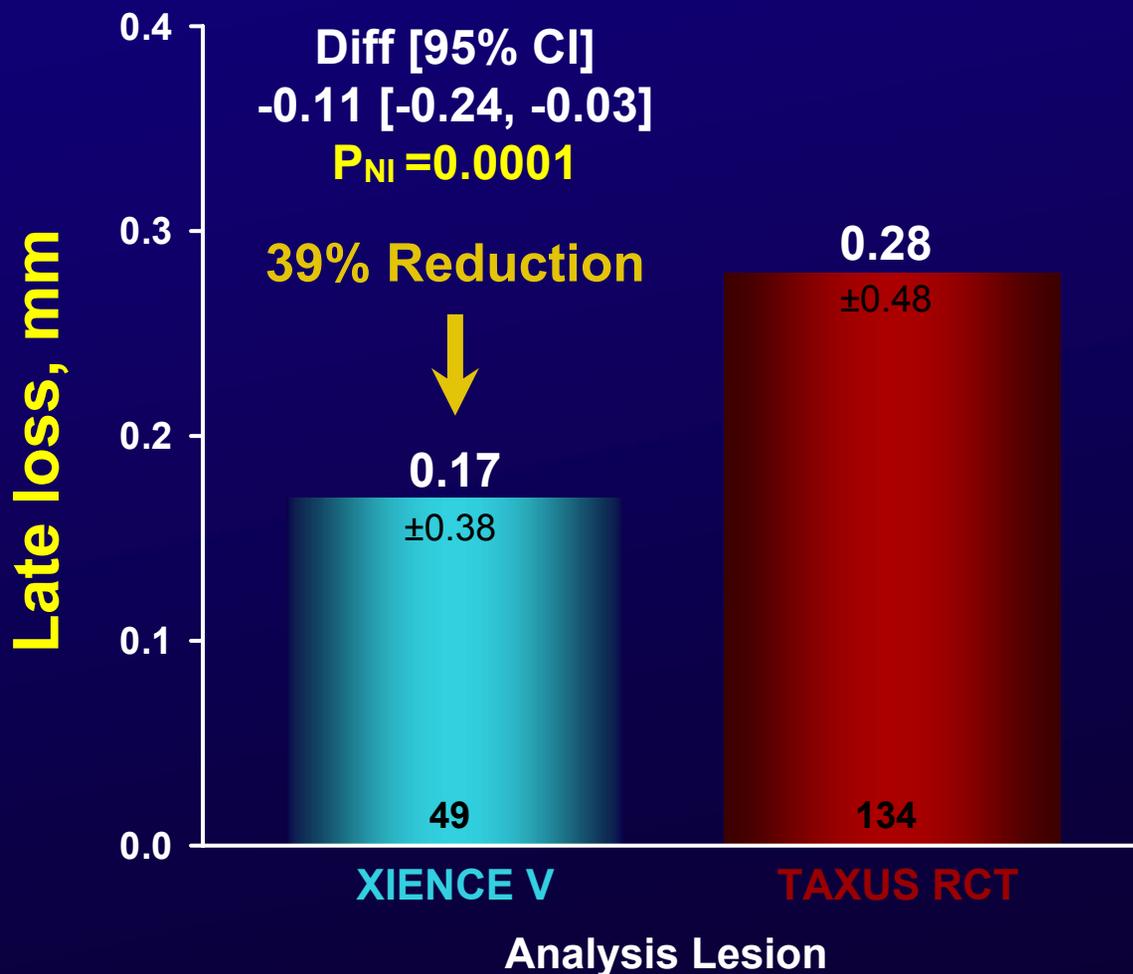
DES vs. DES



* 1 additional patient had angiographic follow-up but baseline angiography was not available

SPIRIT III - 4.0: Primary Endpoint In-segment LL at 8 Months*

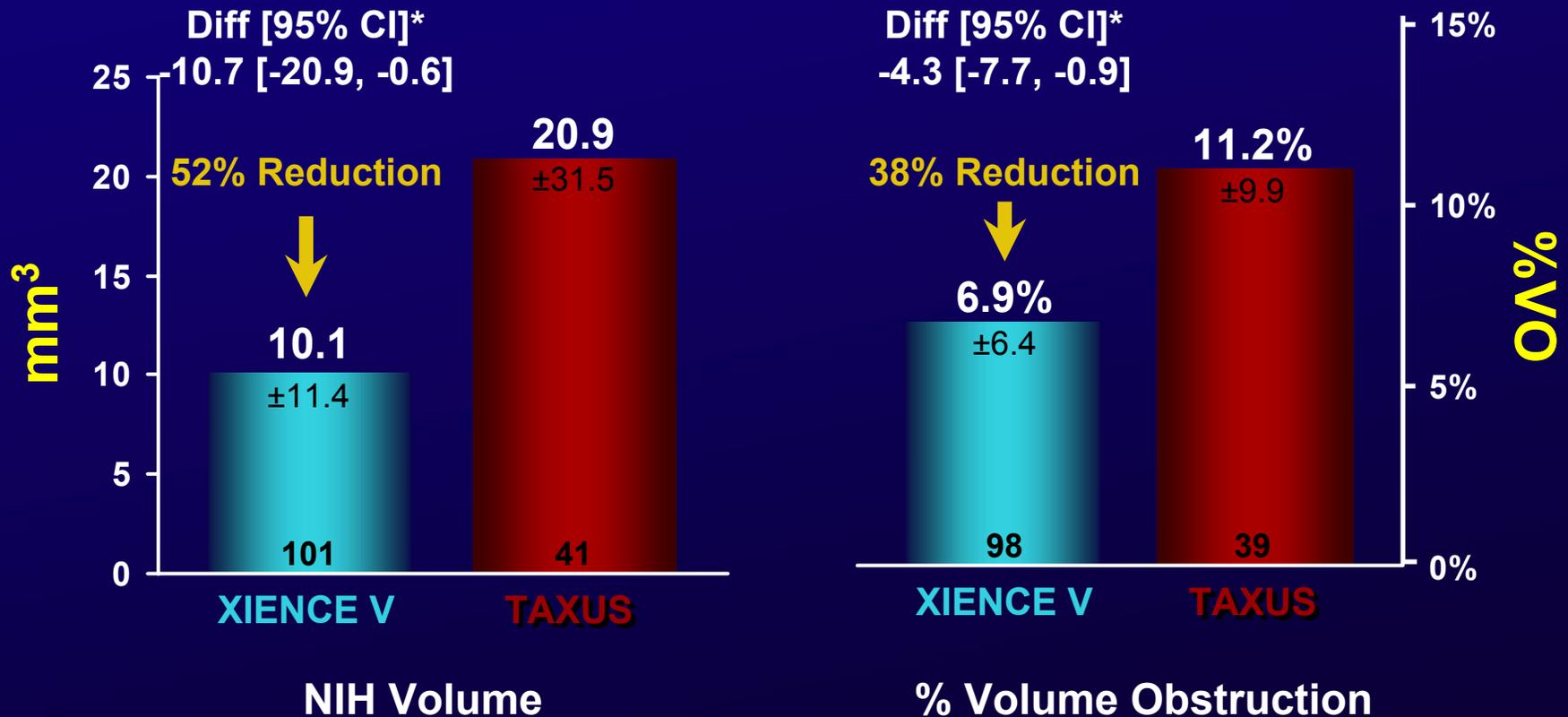
DES vs. DES



* Interim analysis

SPIRIT III: IVUS In-stent Measures at 8 Months

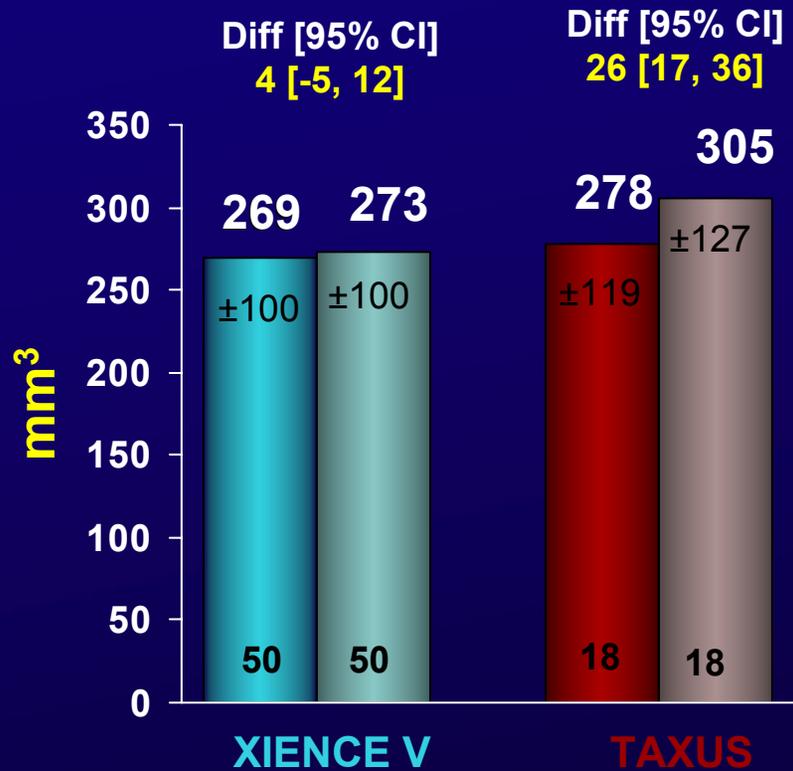
DES vs. DES



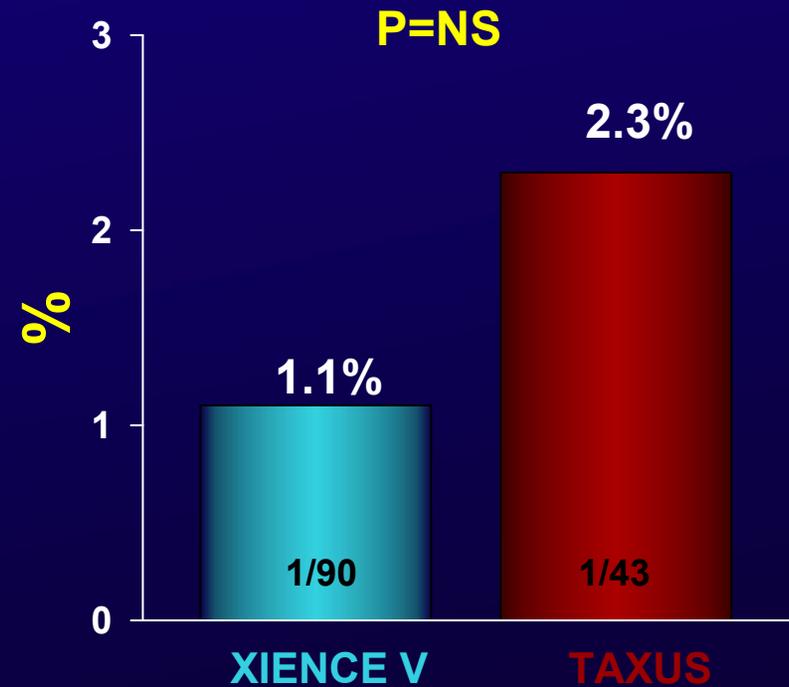
* Confidence Intervals are for descriptive purposes only and not adjusted for multiple comparisons

SPIRIT III: IVUS In-stent Measures at 8 Months

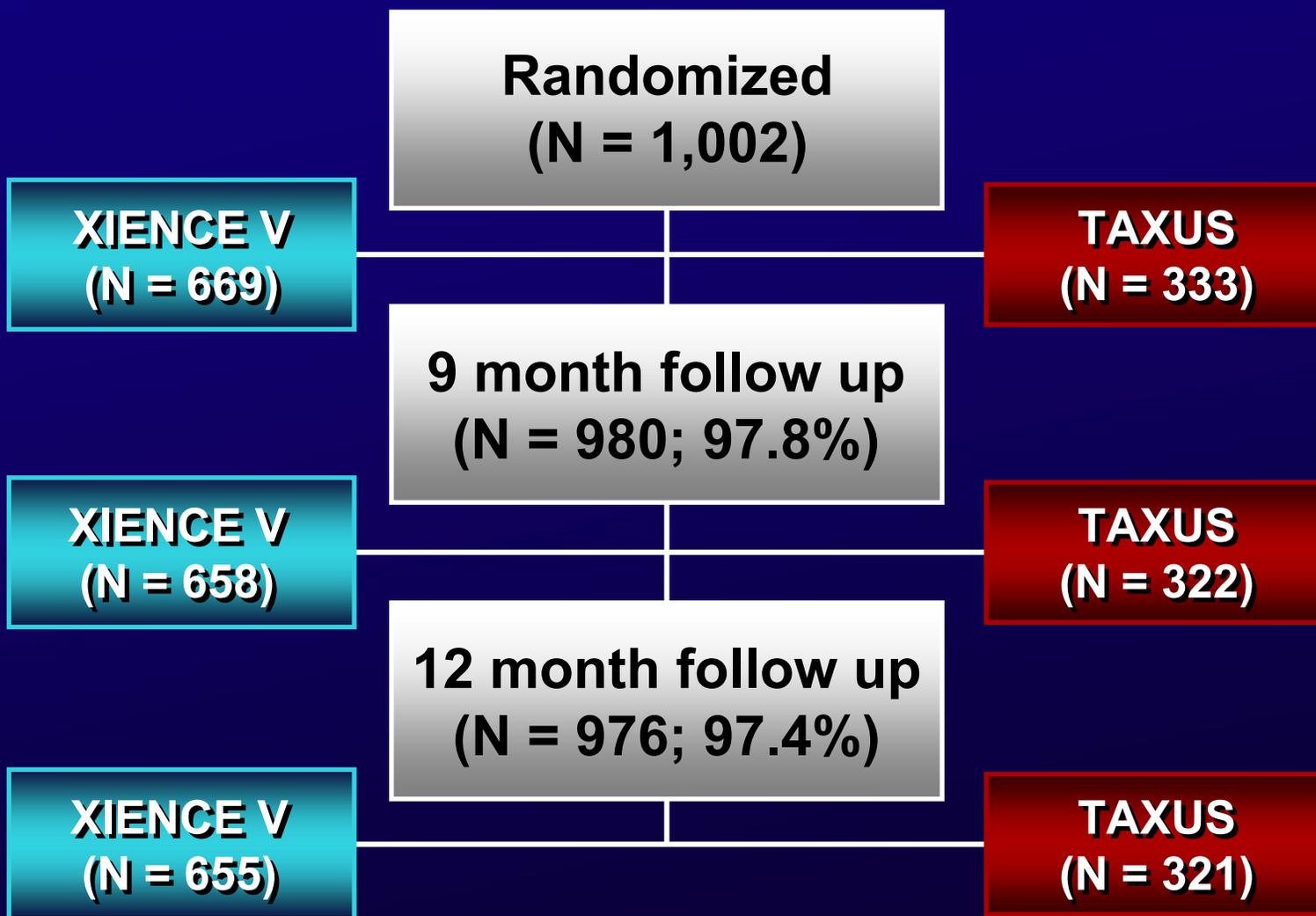
EEL volume post-procedure and at 240 days



Late Acquired Incomplete Apposition

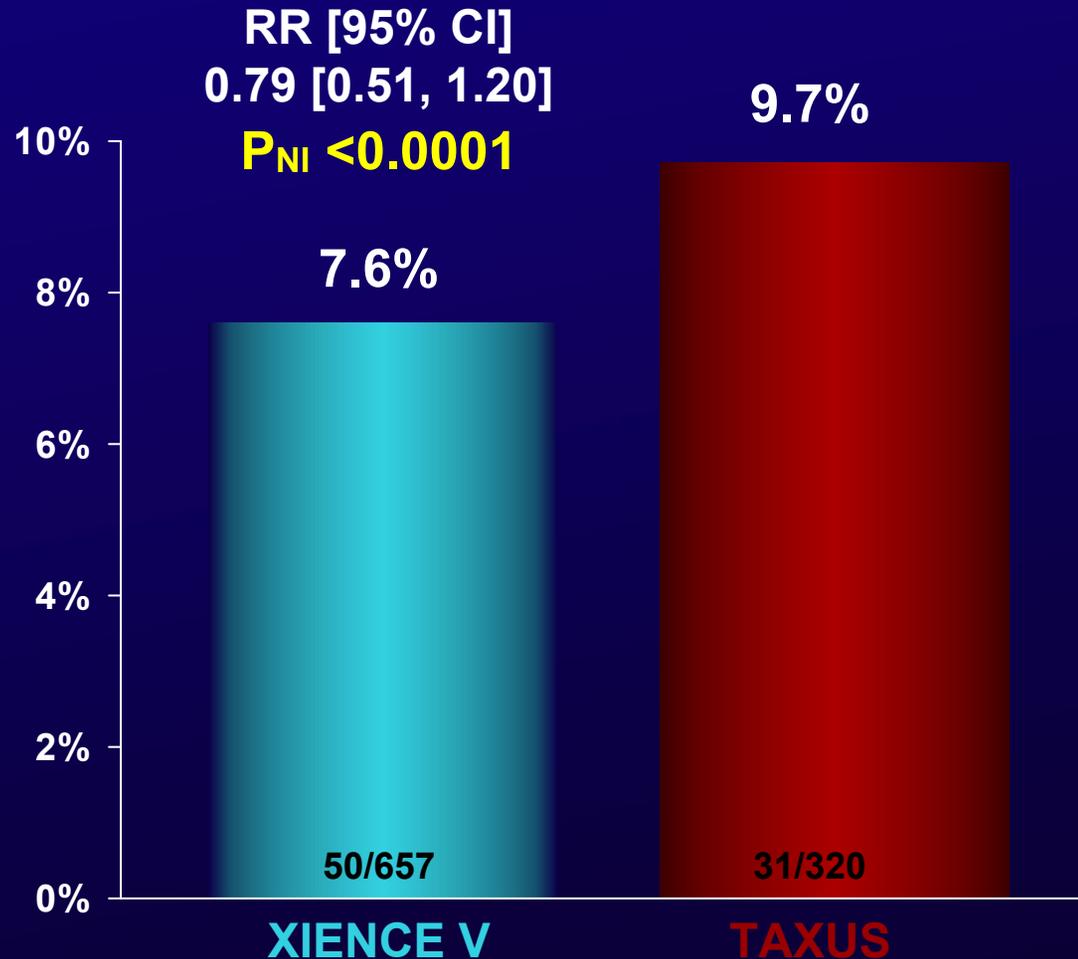


SPIRIT III: Clinical Follow-up

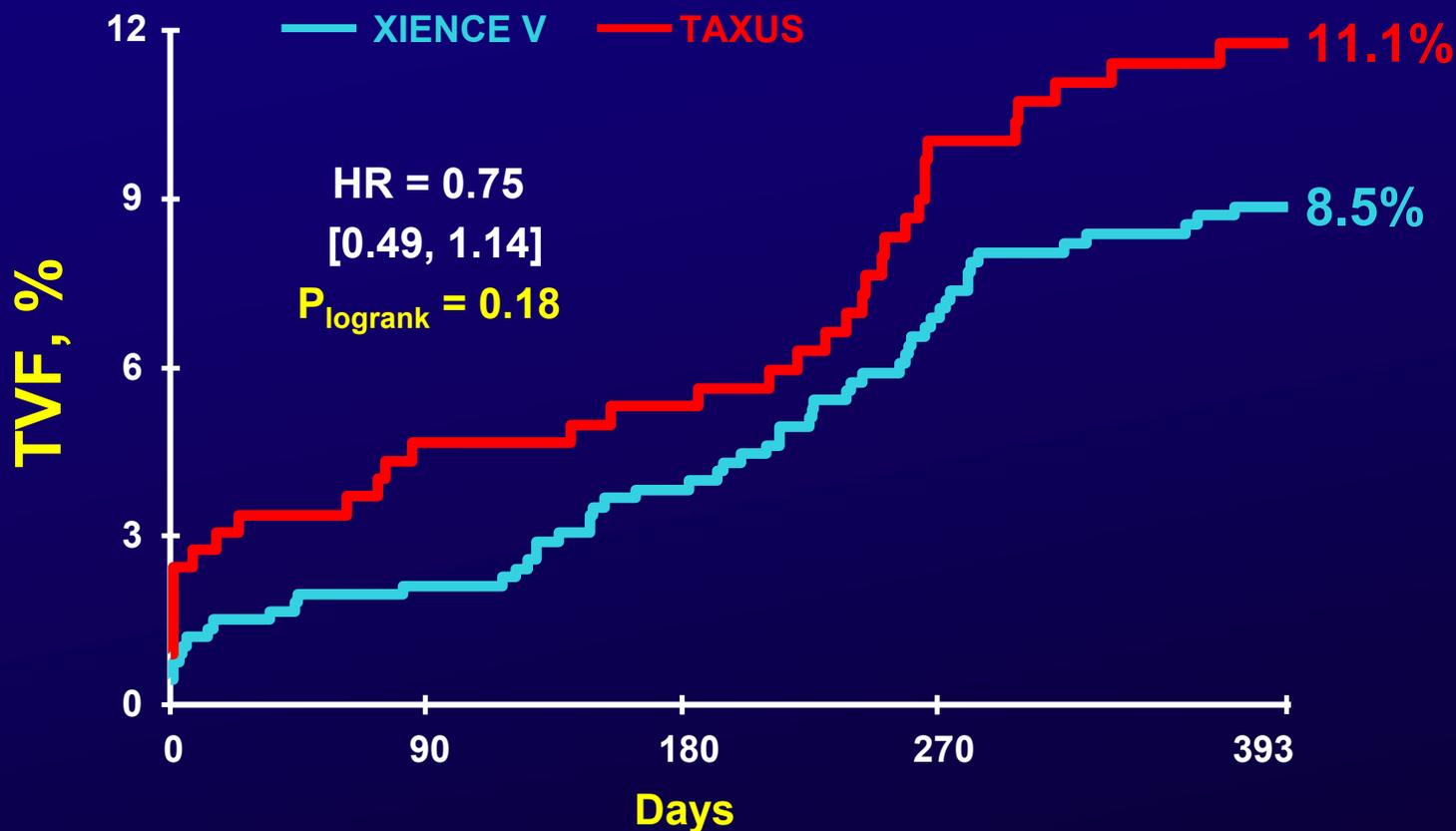


SPIRIT III (Co-Primary Endpoint): TVF at 9 Months

DES vs. DES



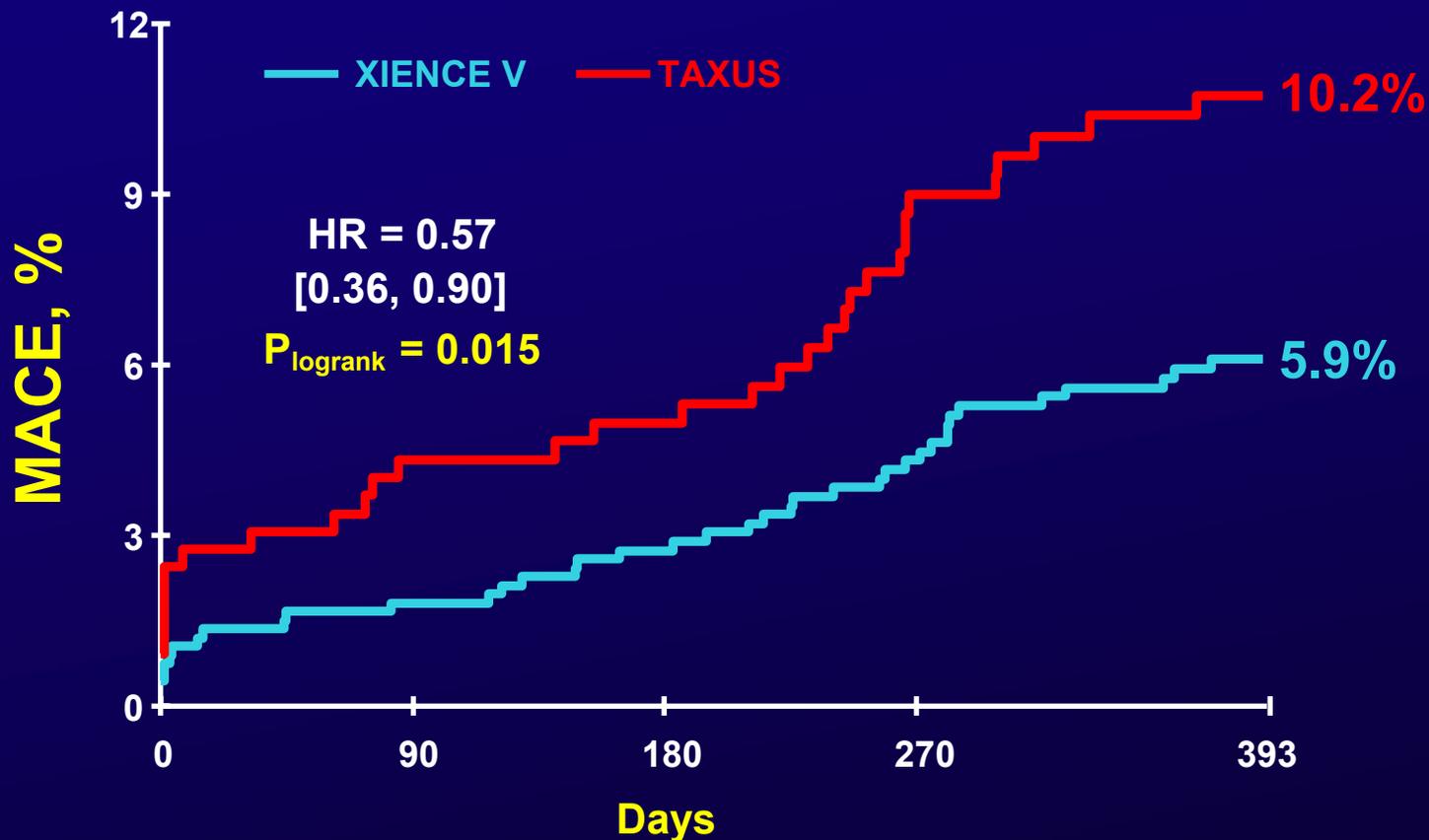
SPIRIT III: TVF at One Year



Number at Risk

XIENCE V	669	649	636	611	597
TAXUS	332	311	308	289	283

SPIRIT III: MACE at One Year

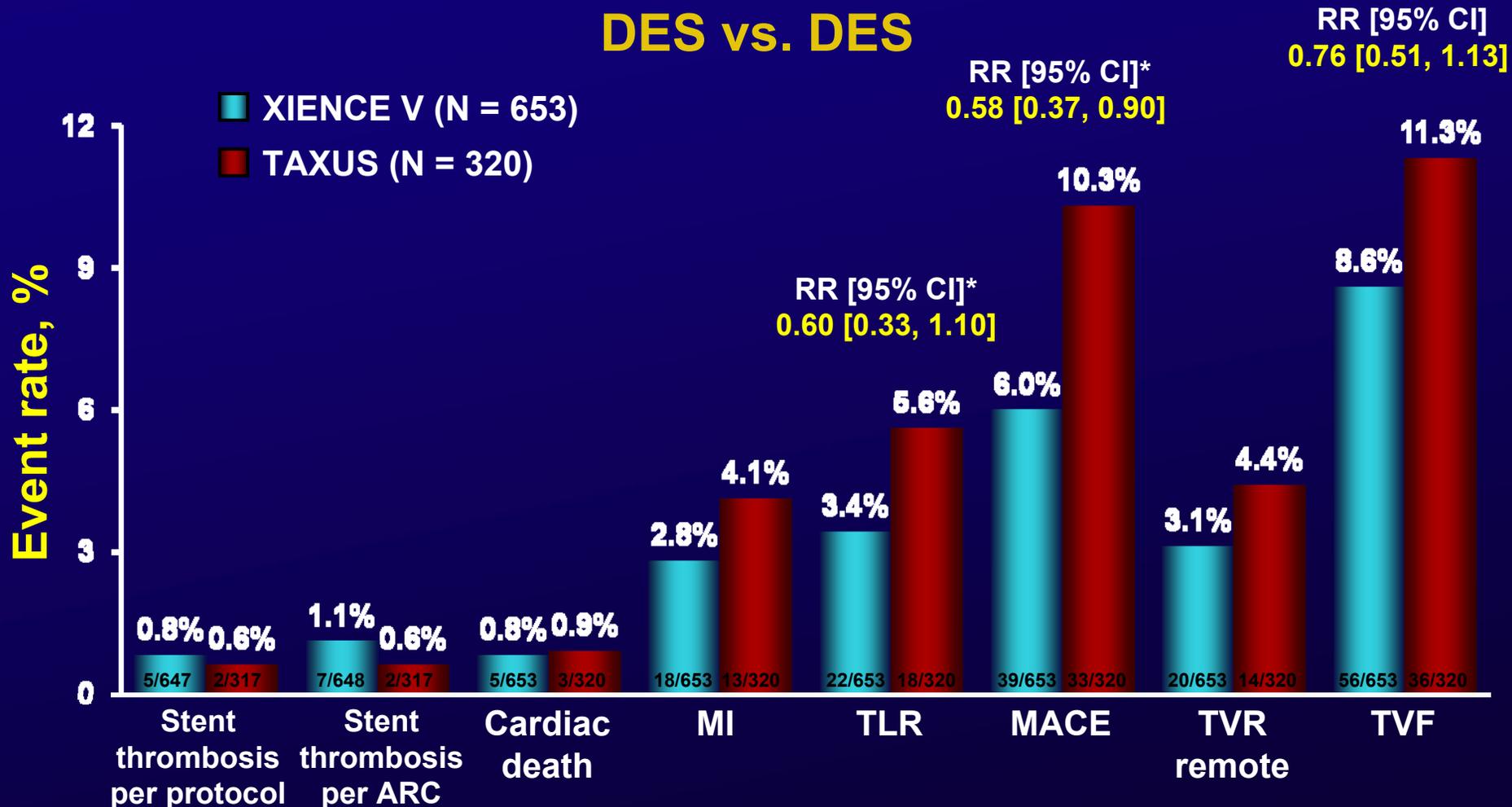


Number at Risk

XIENCE V	669	651	642	626	613
TAXUS	332	312	309	292	286

SPIRIT III: One Year Results

Event Rates



MACE = Cardiac death, MI, or ischemic TLR
 TVF = Cardiac death, MI, or ischemic TVR

* Confidence Intervals for TLR and MACE are for descriptive purposes only and not adjusted for multiple comparisons

Conclusions

SPIRIT III

The pivotal SPIRIT III Trial **met both its pre-specified primary and major secondary (co-primary) endpoints**, demonstrating **superiority** of the XIENCE V stent compared to the TAXUS stent in reducing angiographic in-segment late loss, and **non-inferiority** with regard to the 9 month endpoint of target vessel failure

XIENCE V vs. TAXUS DES vs. DES

SPIRIT II & III Pooled Meta-Analysis

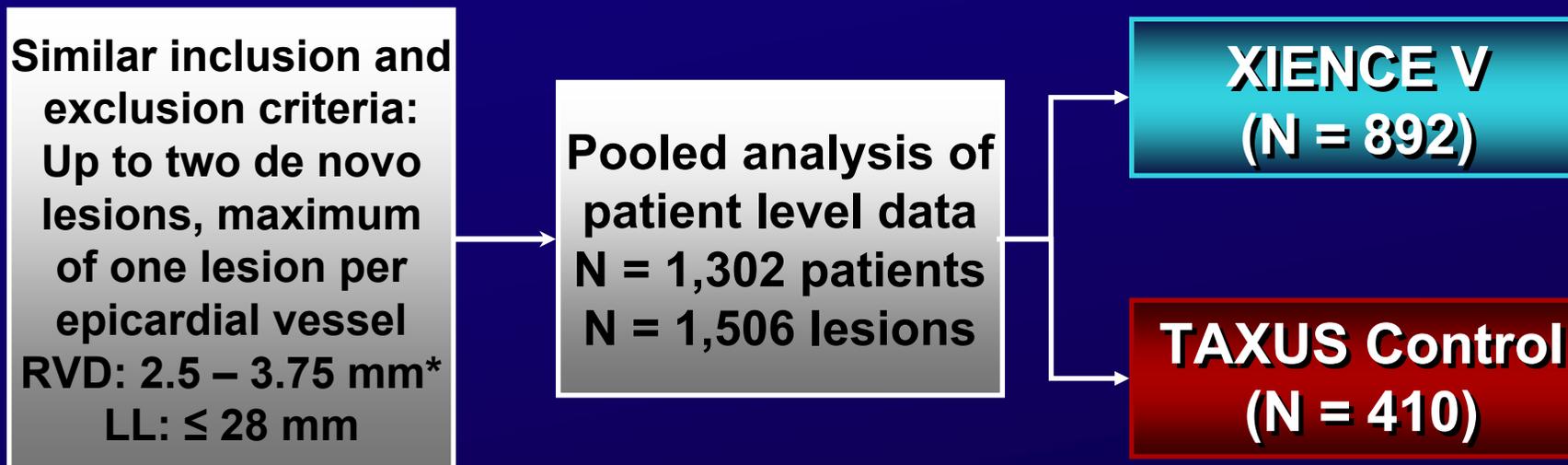
Rationale for the SPIRIT II & III Pooled Analysis

- At the time the SPIRIT III trial was designed, the regulatory burden that was agreed upon with FDA for approval of the XIENCE V stent was the demonstration of non-inferiority for angiographic late loss and target vessel failure compared to TAXUS, which required randomization of 1,002 patients
- Since that time interest has shifted to examination of lower frequency safety and efficacy endpoints, such as death, MI, stent thrombosis and TLR
 - SPIRIT III was not powered to examine the rates of these endpoints

Rationale for the SPIRIT II & III Pooled Analysis

- Thus, at the request of FDA, to provide more power to examine infrequent events, we have combined SPIRIT II and III in a true patient level pooled meta-analysis
 - In SPIRIT II and III, patients with similar inclusion and exclusion criteria were randomized in 2 consecutive randomized trials to XIENCE V vs. TAXUS – follow-up has been completed to 1 year in both trials

SPIRIT II & III Pooled Analysis



- Two prospective, single blind trials with similar inclusion and exclusion criteria in 1,302 pts with 1,506 lesions
- Independent pooled analysis by academic statisticians at the Cardiovascular Research Foundation
- Pre-specified superiority testing on all endpoints
- All analyses are exploratory and hypothesis generating

SPIRIT II & III Meta-Analysis

Baseline Characteristics (N = 1,302 pts)

	XIENCE V (N = 892 pts)	TAXUS (N = 410 pts)
Age (years)	62.9 ± 10.5	62.6 ± 10.1
Male	70.3%	68.2%
Diabetes	27.9%	27.1%
- treated with insulin	7.1%	5.7%
Hypertension	74.0%	72.3%
Hypercholesterolemia	72.8%	72.1%
Current smoker	25.3%	23.8%
Prior MI	23.7%	19.3%
Unstable angina	20.8%	26.5%
Dual vessel treatment	15.7%	15.9%

SPIRIT II & III Meta-Analysis

Angiographic Characteristics (N = 1,506 lesions)*

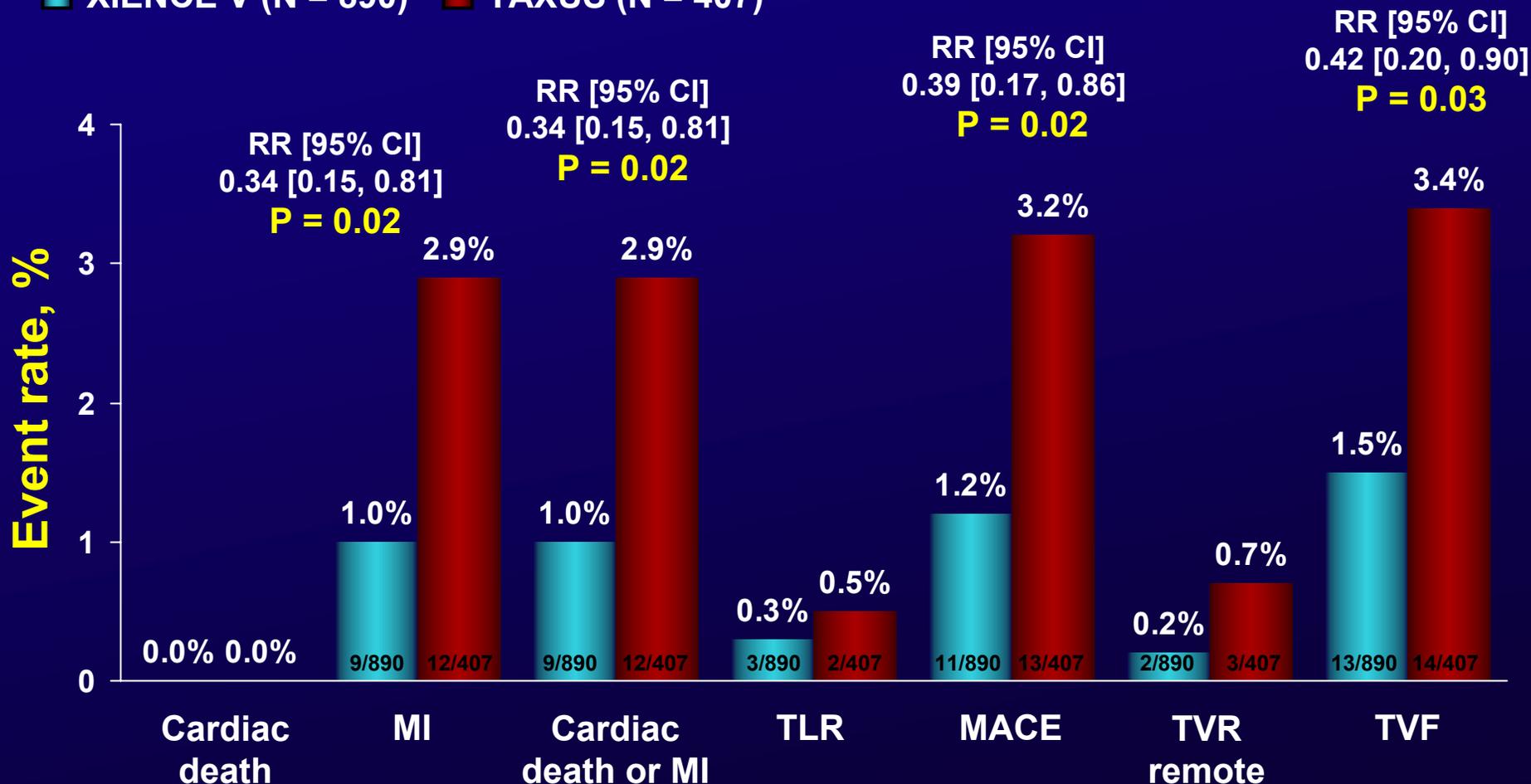
		XIENCE V	TAXUS
		(N = 1,028 lesions)	(N = 473 lesions)
Lesion Location	LAD	41.1%	43.8%
	LCX	28.0%	26.4%
	RCA	30.7%	29.6%
	LMCA	0.1%	0.2%
QCA	RVD (mm)	2.75 ± 0.47	2.77 ± 0.48
	MLD (mm)	0.88 ± 0.43	0.89 ± 0.41
	DS (%)	67.7 ± 13.6	67.5 ± 13.6
	Lesion length (mm)	14.3 ± 5.7	14.5 ± 5.9

* Information on 5 lesions was not available

SPIRIT II & SPIRIT III Meta-Analysis

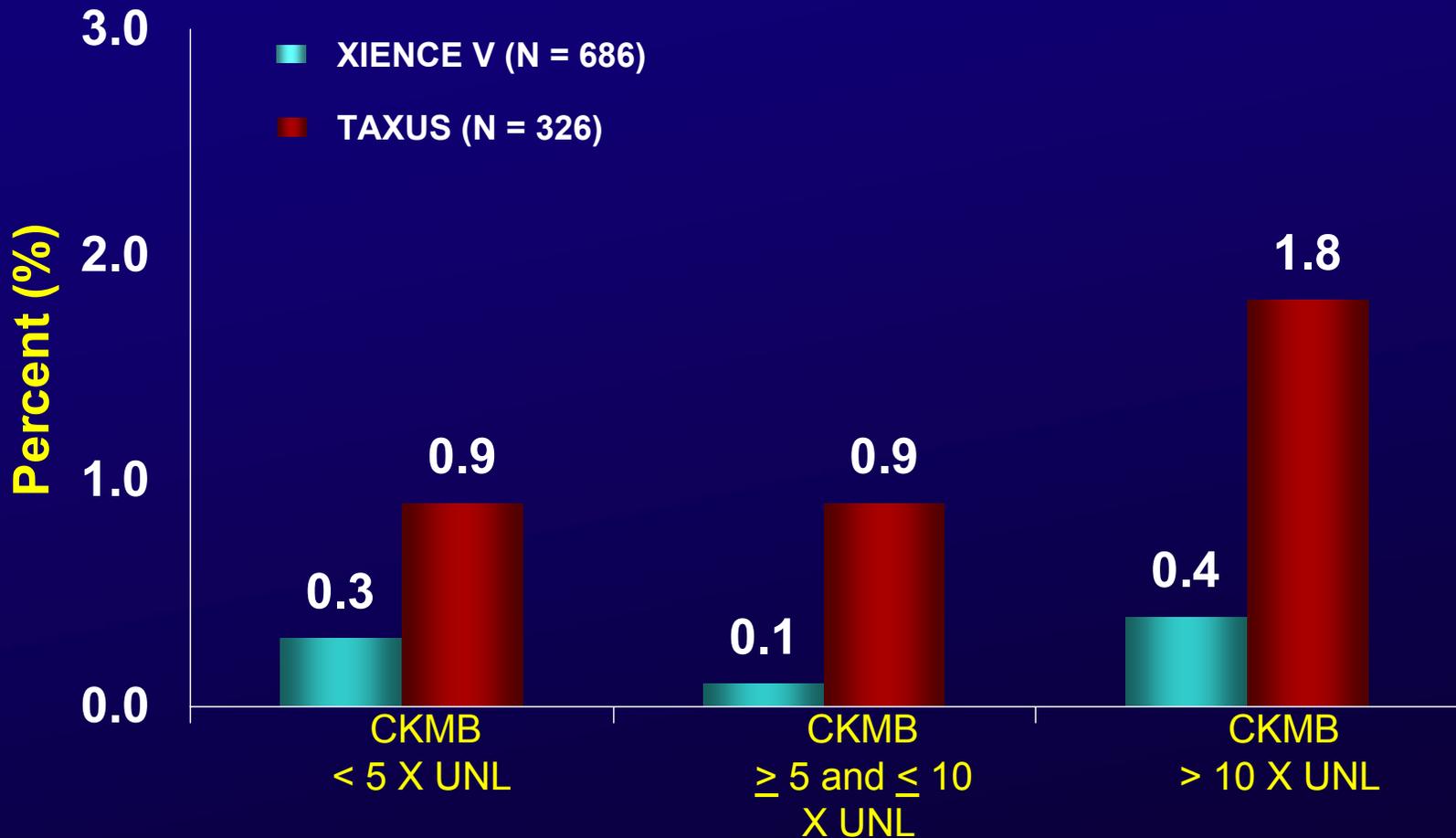
Event Rates at 30 (± 7) Days

■ XIENCE V (N = 890) ■ TAXUS (N = 407)



MACE = Cardiac death, MI, or ischemic TLR
 TVF = Cardiac death, MI, or ischemic TVR

SPIRIT II & III Pooled Analysis NQMI (CKMB Rises) through 37 Days



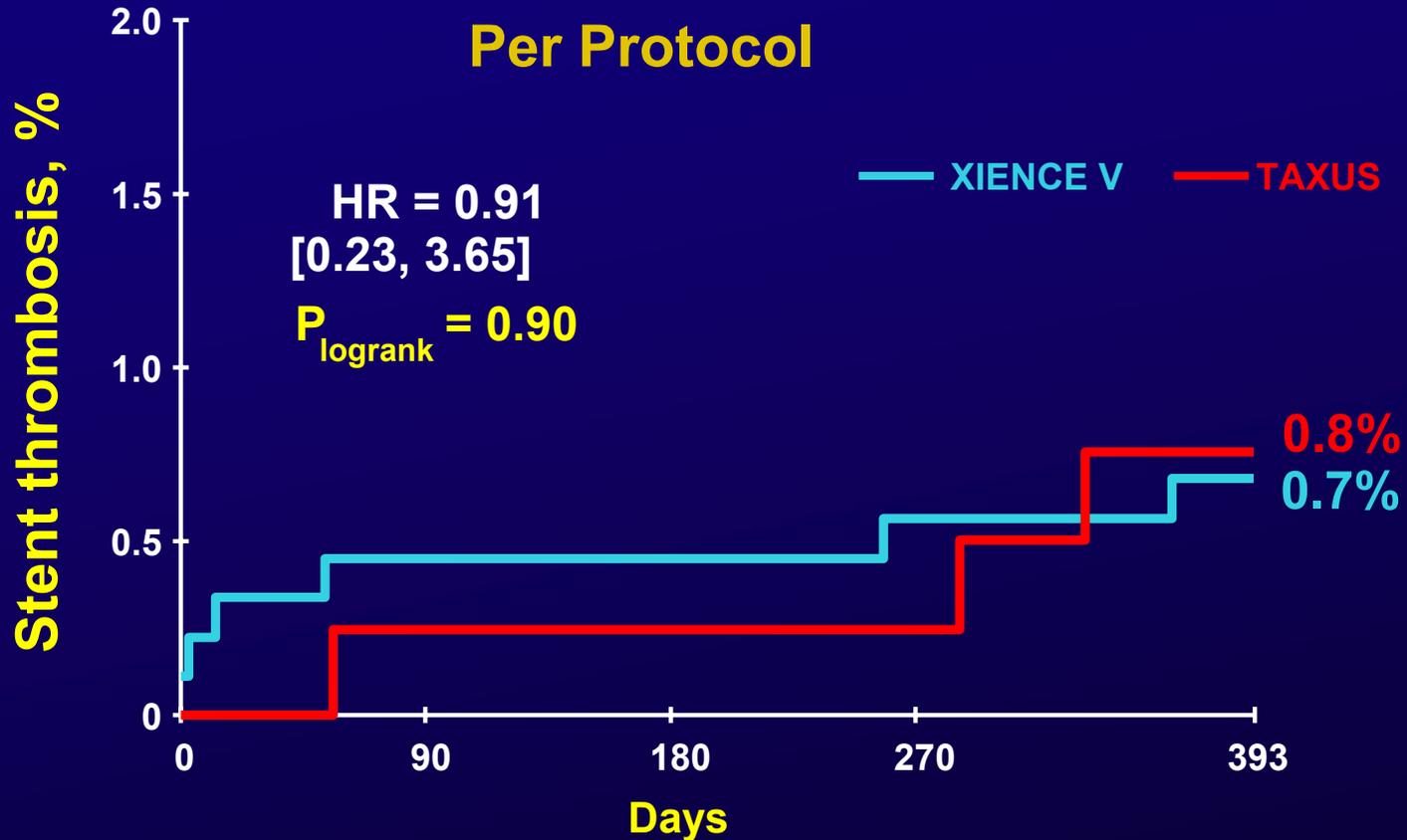
Results for subjects with post-procedure CKMB values available

Note: Three XIENCETM V subjects had NQMI within 37 days post procedure

but did not have post-procedure CKMB value, therefore they are excluded from this analysis.

SPIRIT II & III Meta-Analysis

Stent Thrombosis Through One Year

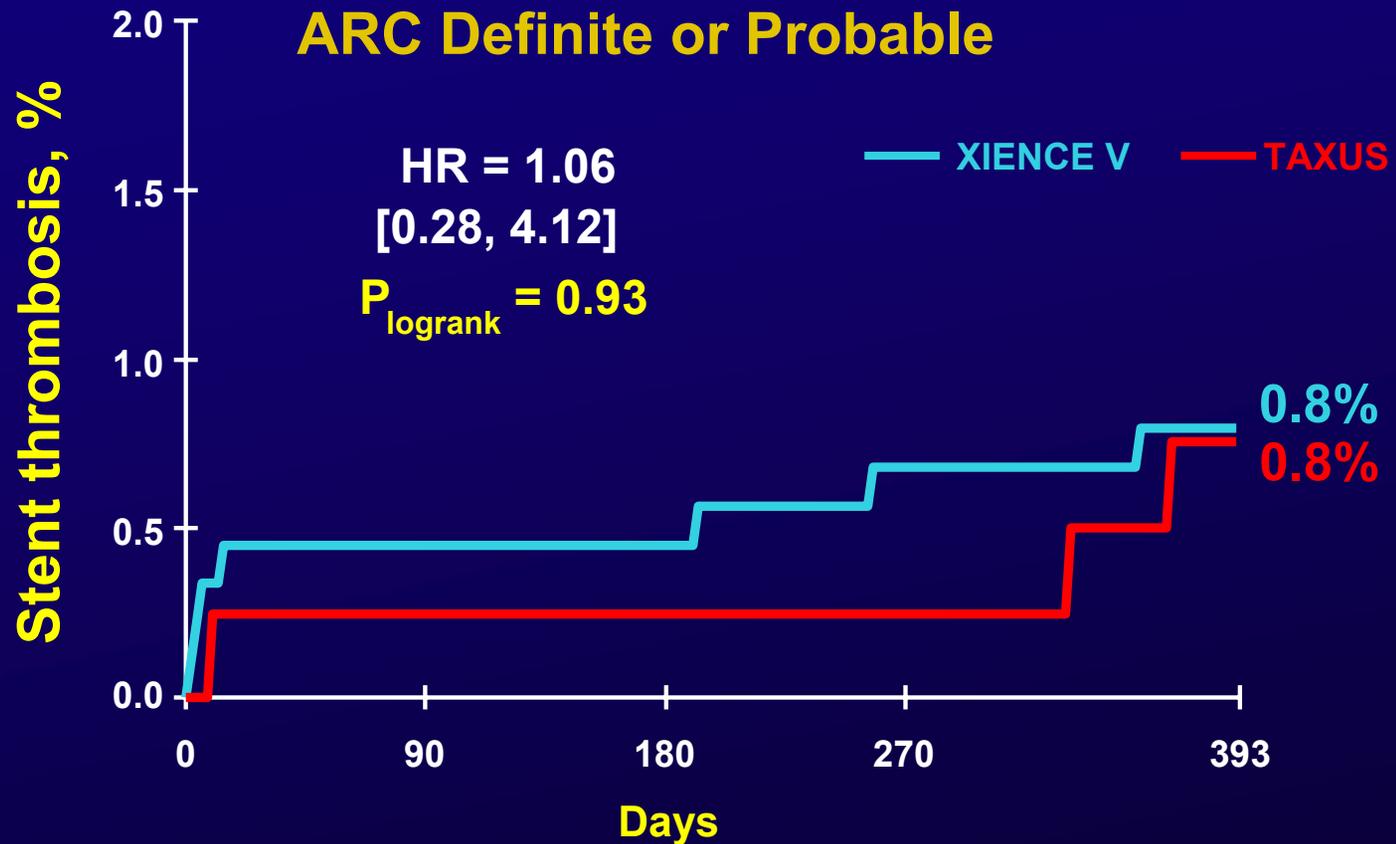


Number at Risk

XIENCE V	892	881	878	867	861
TAXUS	409	401	400	394	390

SPIRIT II & III Meta-Analysis

Stent Thrombosis Through One Year

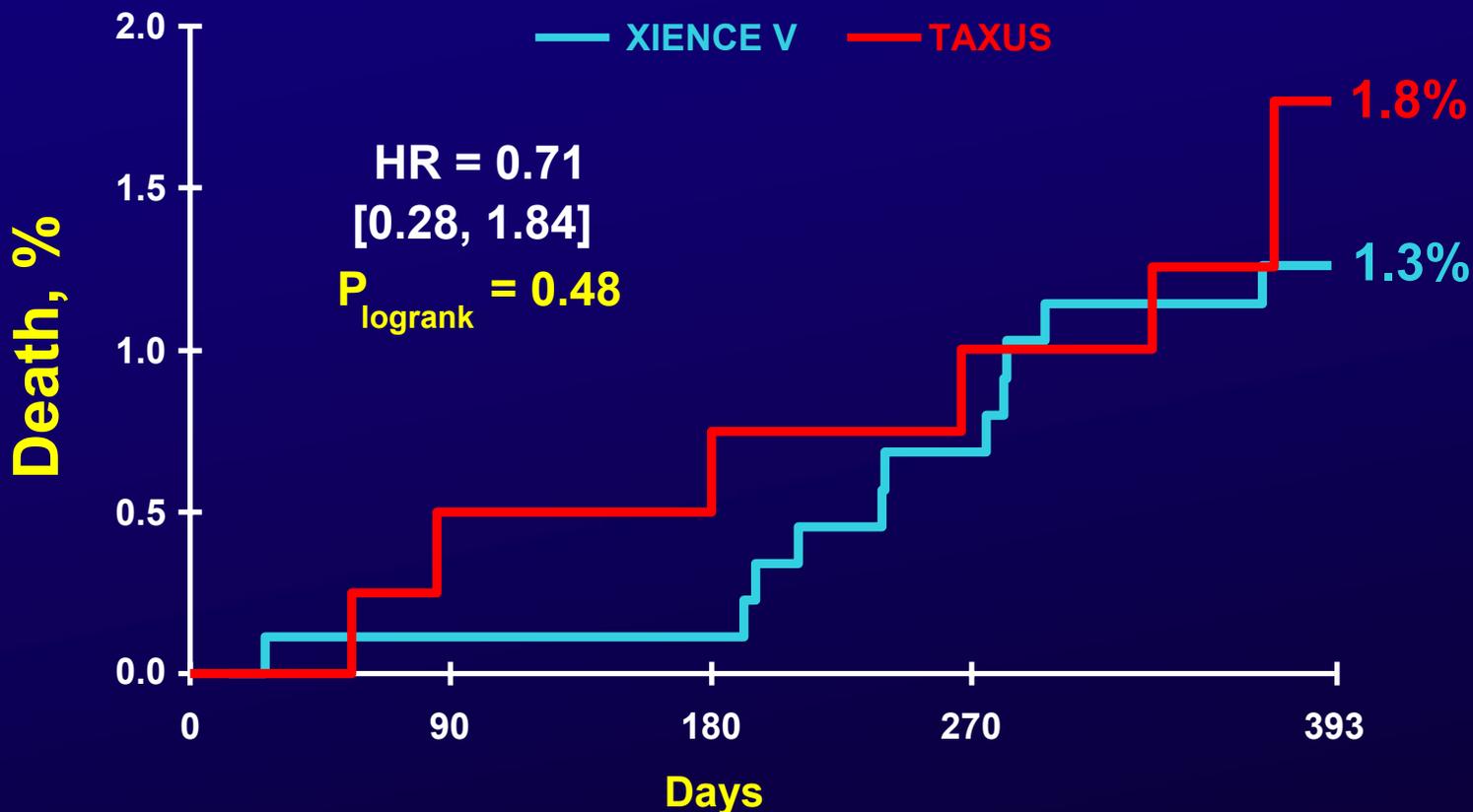


Number at Risk

XIENCE V	892	881	878	867	861
TAXUS	409	401	400	394	390

SPIRIT II & III Meta-Analysis

All-Cause Death at One Year

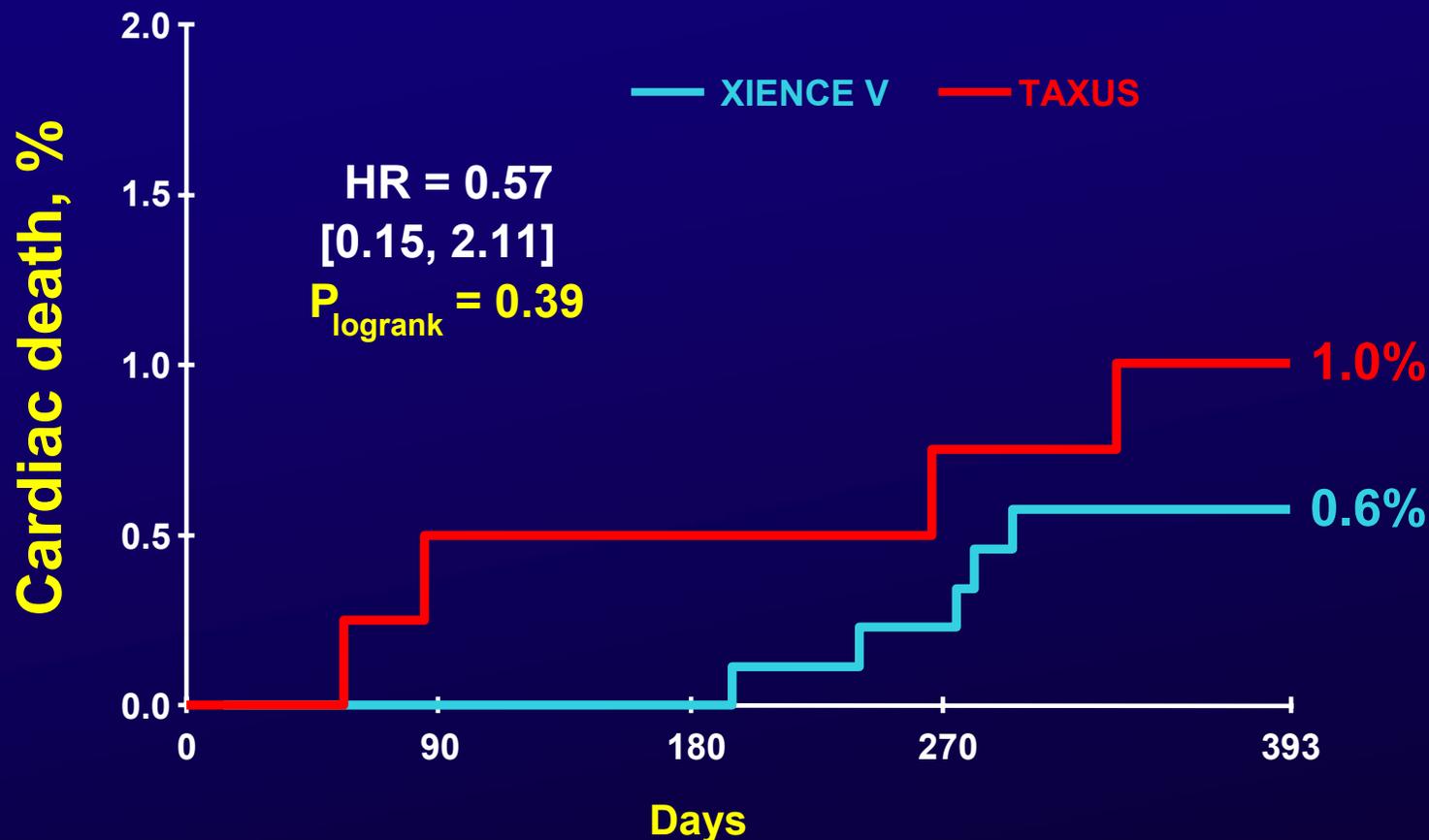


Number at Risk

XIENCE V	892	884	881	871	865
TAXUS	409	401	400	394	389

SPIRIT II & III Meta-Analysis

Cardiac Death at One Year

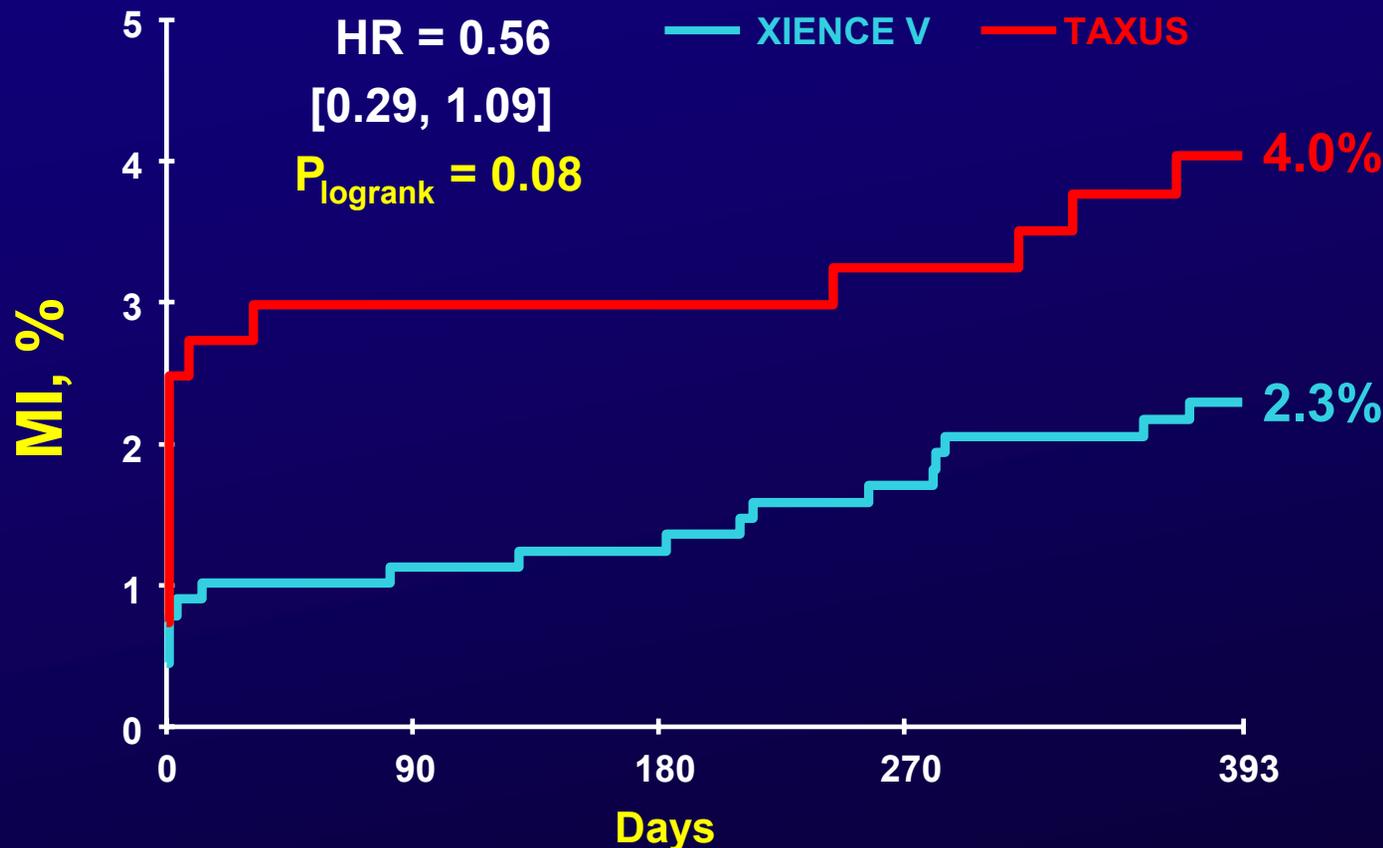


Number at Risk

XIENCE V	892	884	881	871	866
TAXUS	409	401	400	394	391

SPIRIT II & III Meta-Analysis

MI at One Year

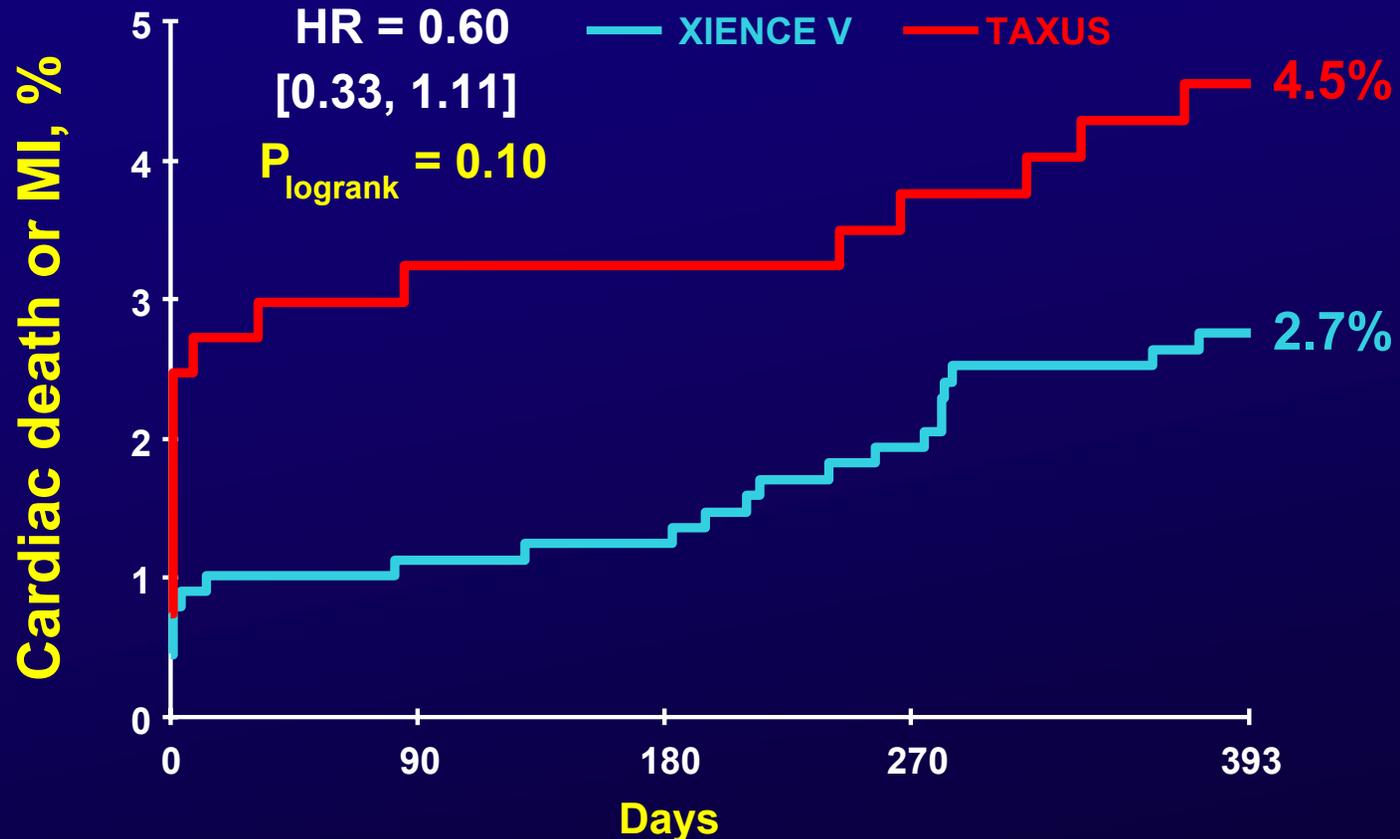


Number at Risk

XIENCE V	892	875	871	857	848
TAXUS	409	390	389	382	378

SPIRIT II & III Meta-Analysis

Cardiac Death or MI at One Year

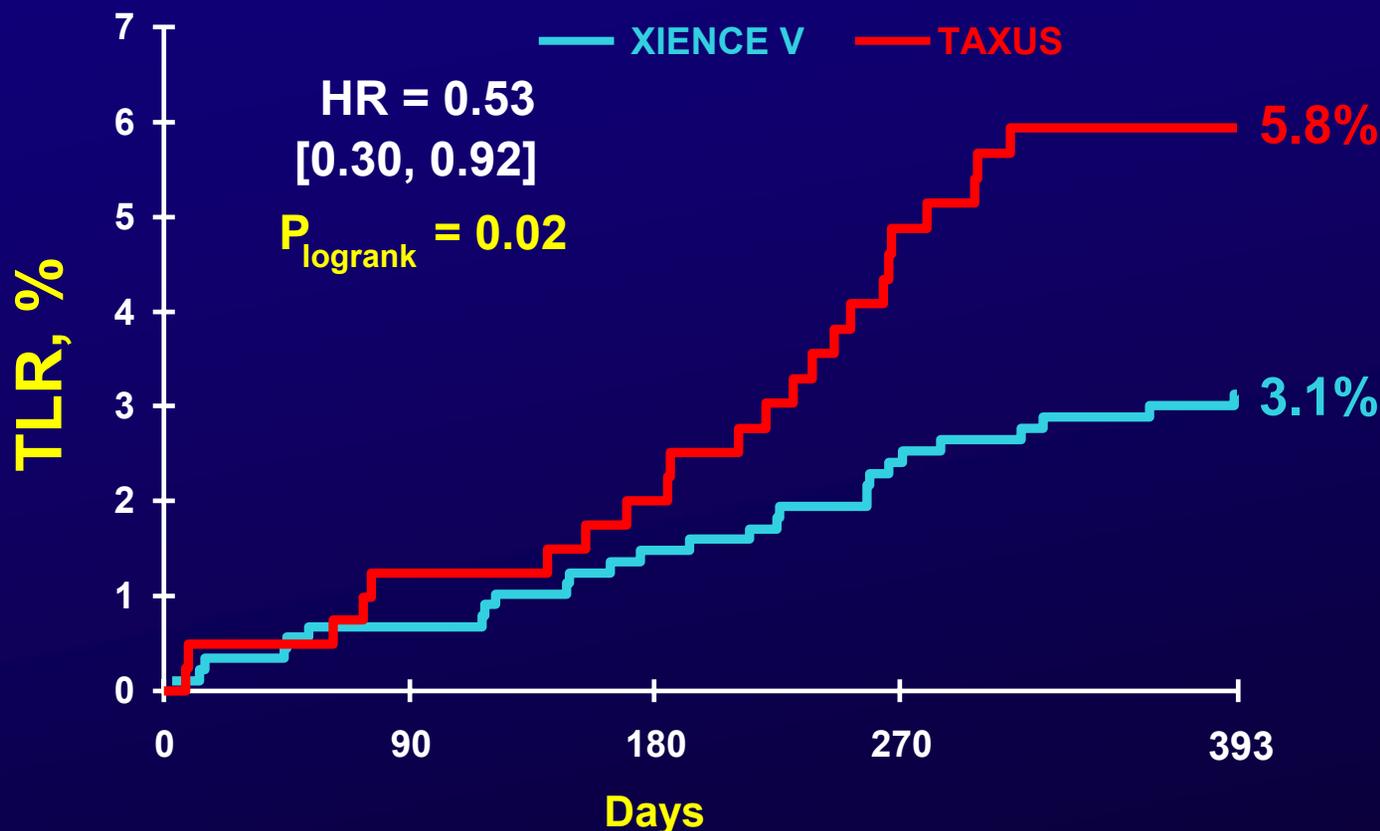


Number at Risk

XIENCE V	892	875	871	857	848
TAXUS	409	390	389	382	378

SPIRIT II & III Meta-Analysis

TLR at One Year



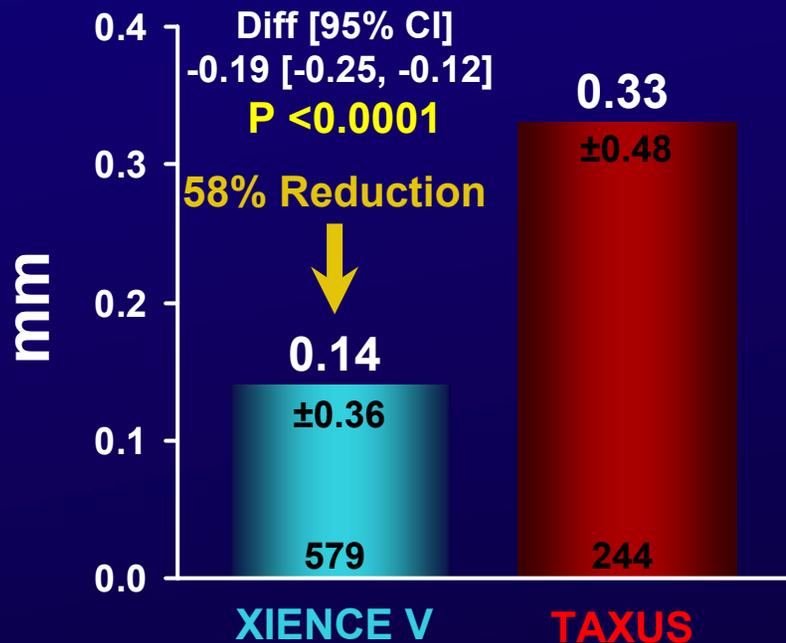
Number at Risk

XIENCE V	892	879	869	851	840
TAXUS	409	397	393	376	369

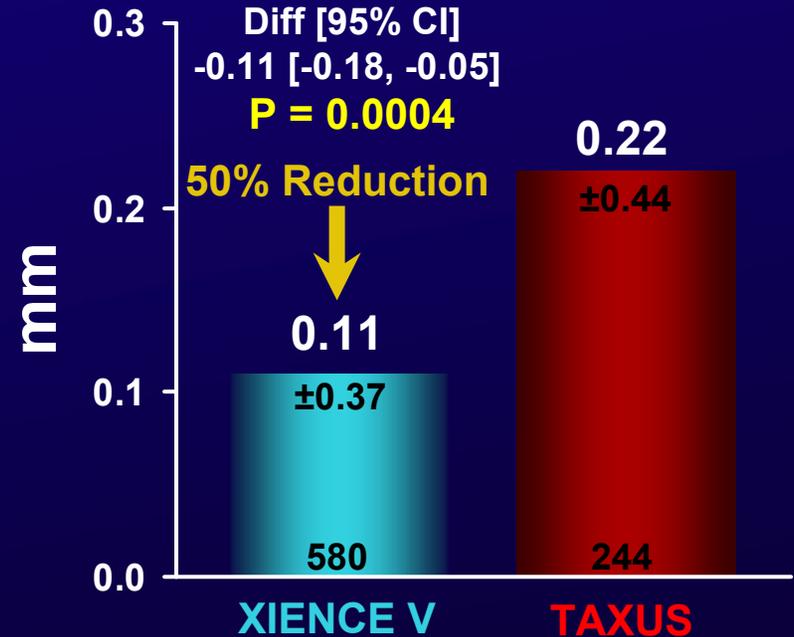
SPIRIT II & III Meta-Analysis

Key Angiographic Endpoints

In-stent late loss



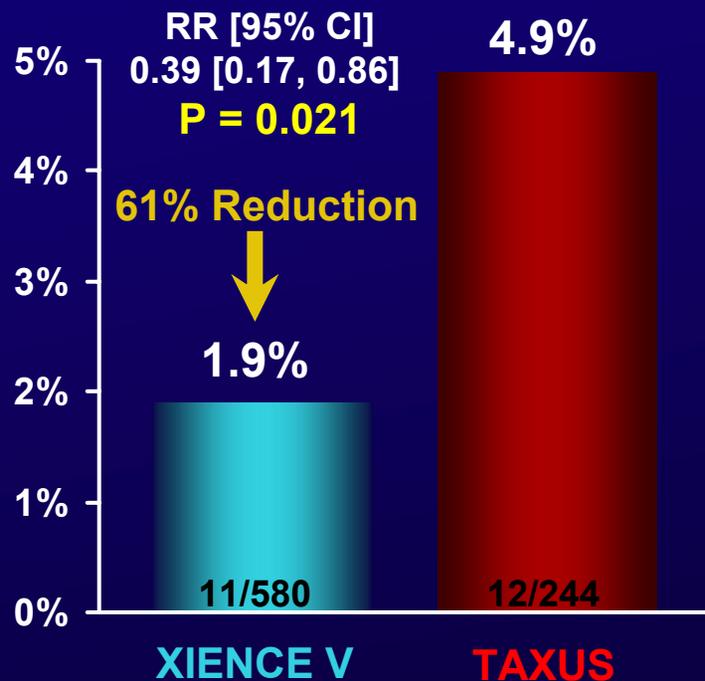
In-segment late loss



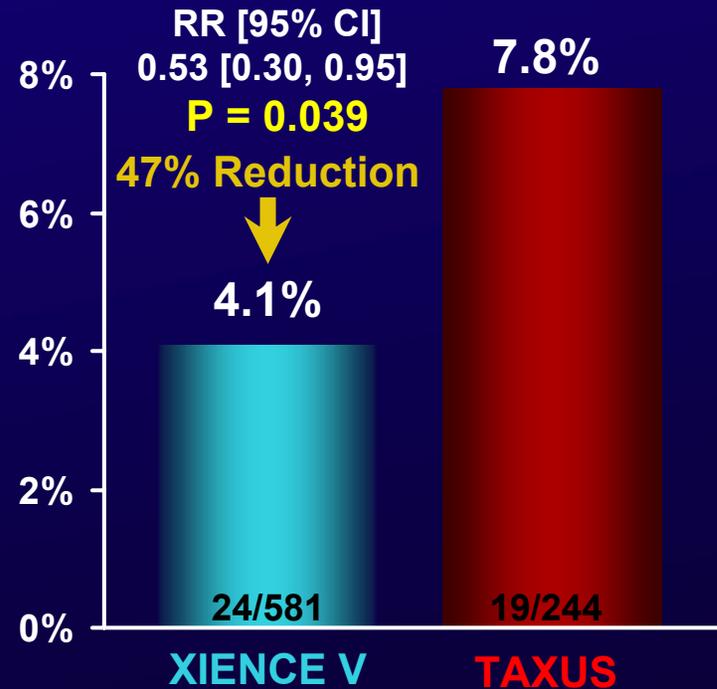
SPIRIT II & III Meta-Analysis

Key Angiographic Endpoints

In-stent binary restenosis

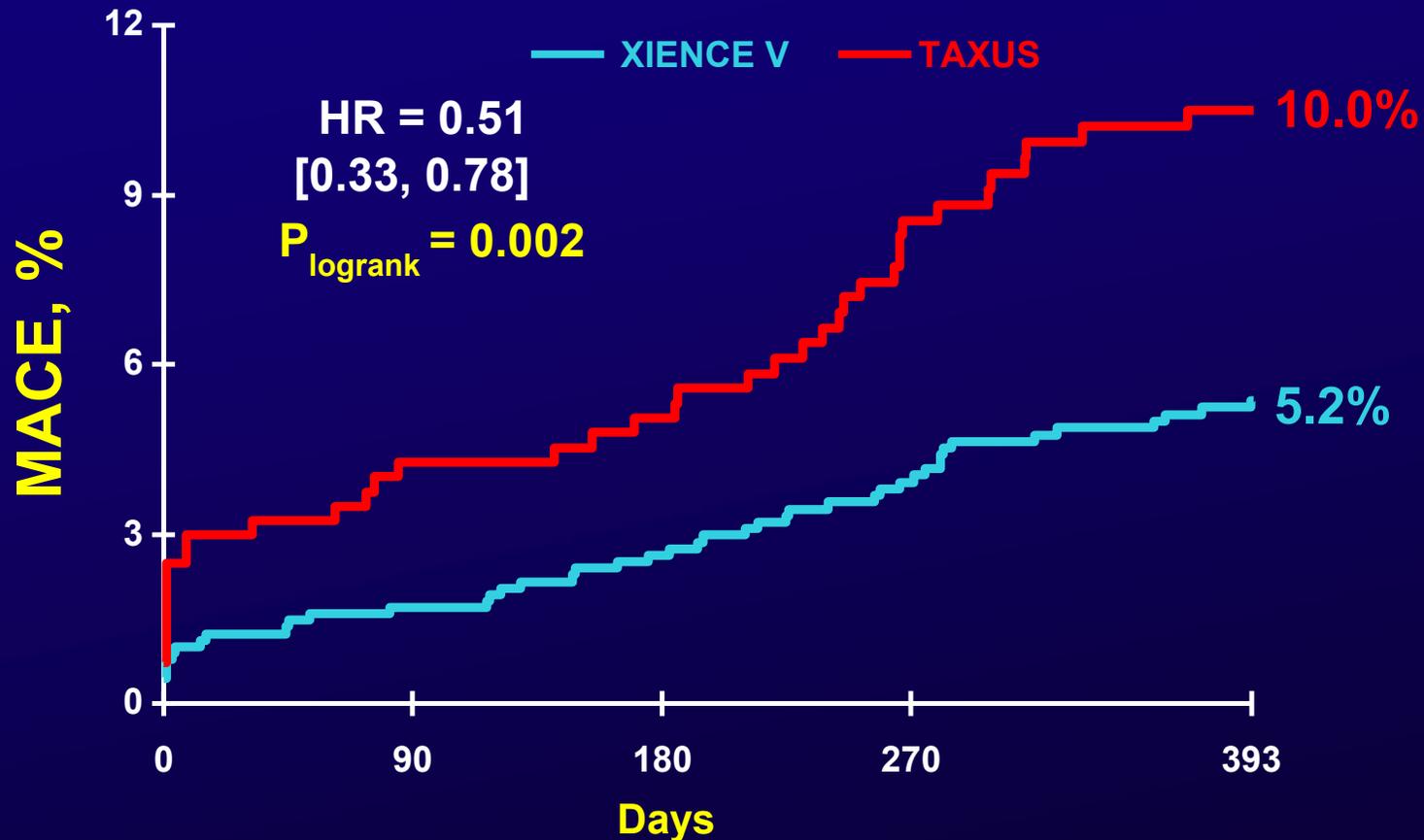


In-segment binary restenosis



SPIRIT II & III Meta-Analysis

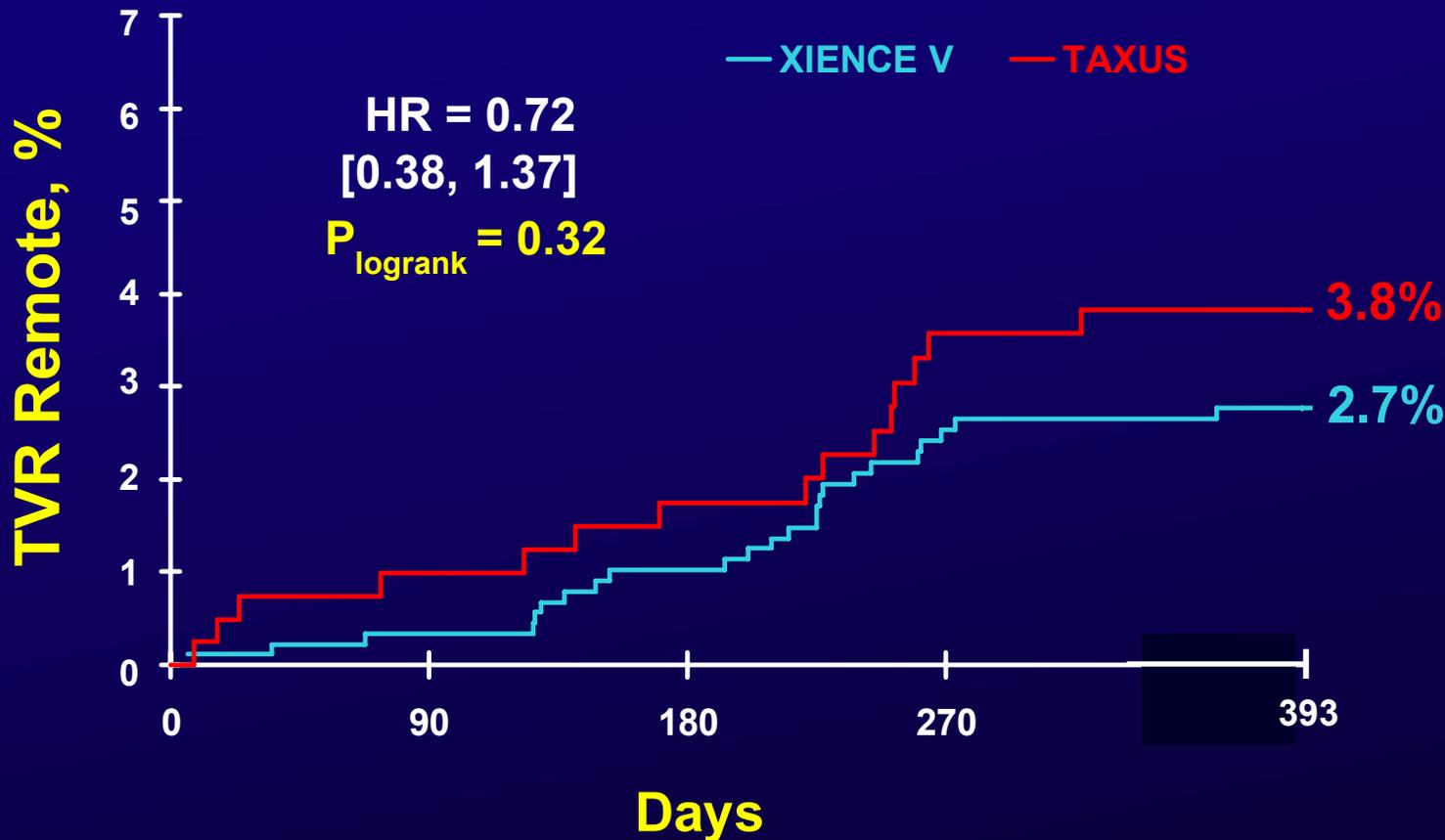
MACE at One Year



Number at Risk

XIENCE V	892	870	859	840	826
TAXUS	409	386	382	364	356

SPIRIT II & III Meta-Analysis TVR Remote at One Year

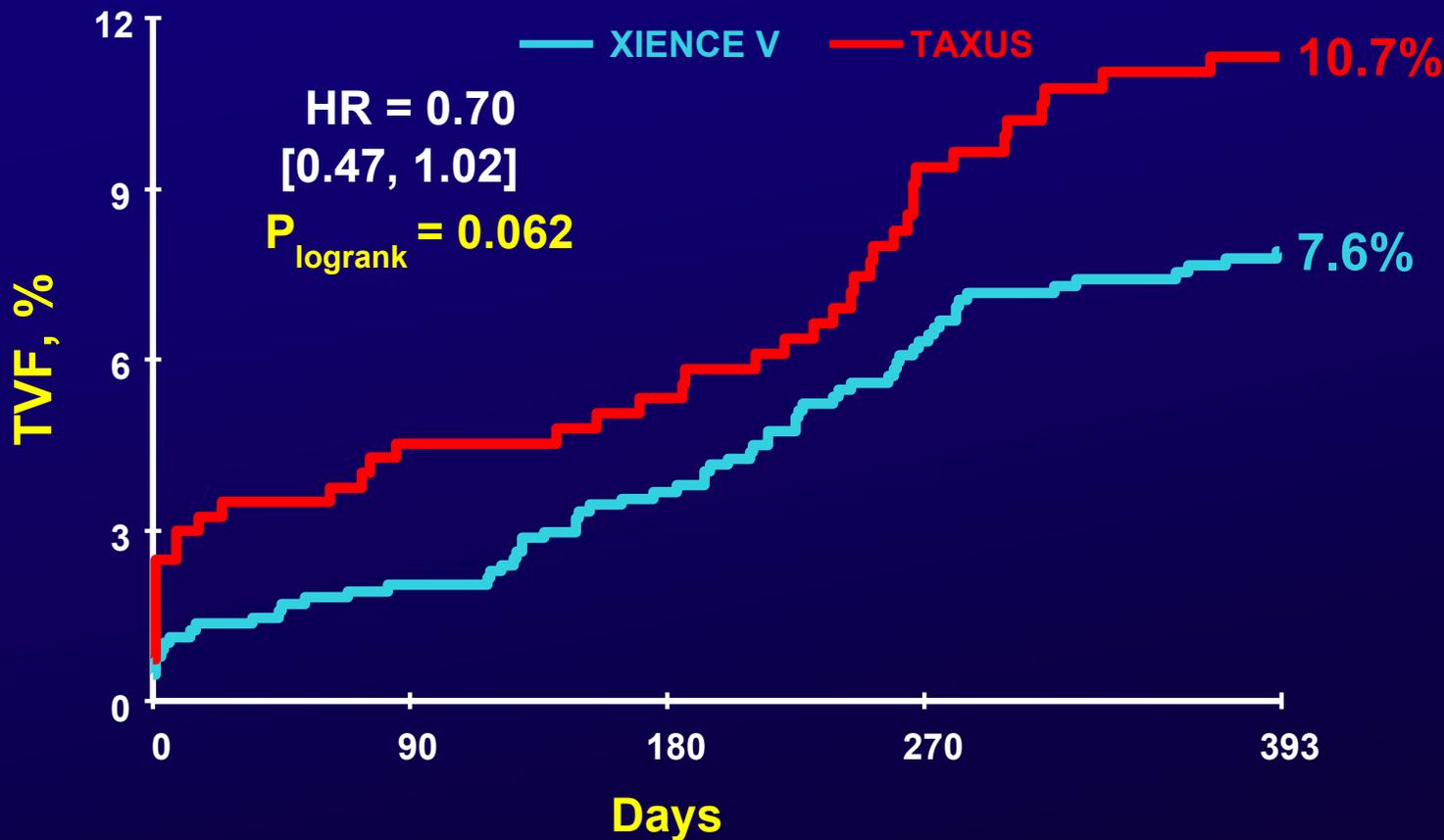


Number at Risk

XIENCE V	892	881	873	850	843
TAXUS	409	397	393	380	377

SPIRIT II & III Meta-Analysis

TVF at One Year



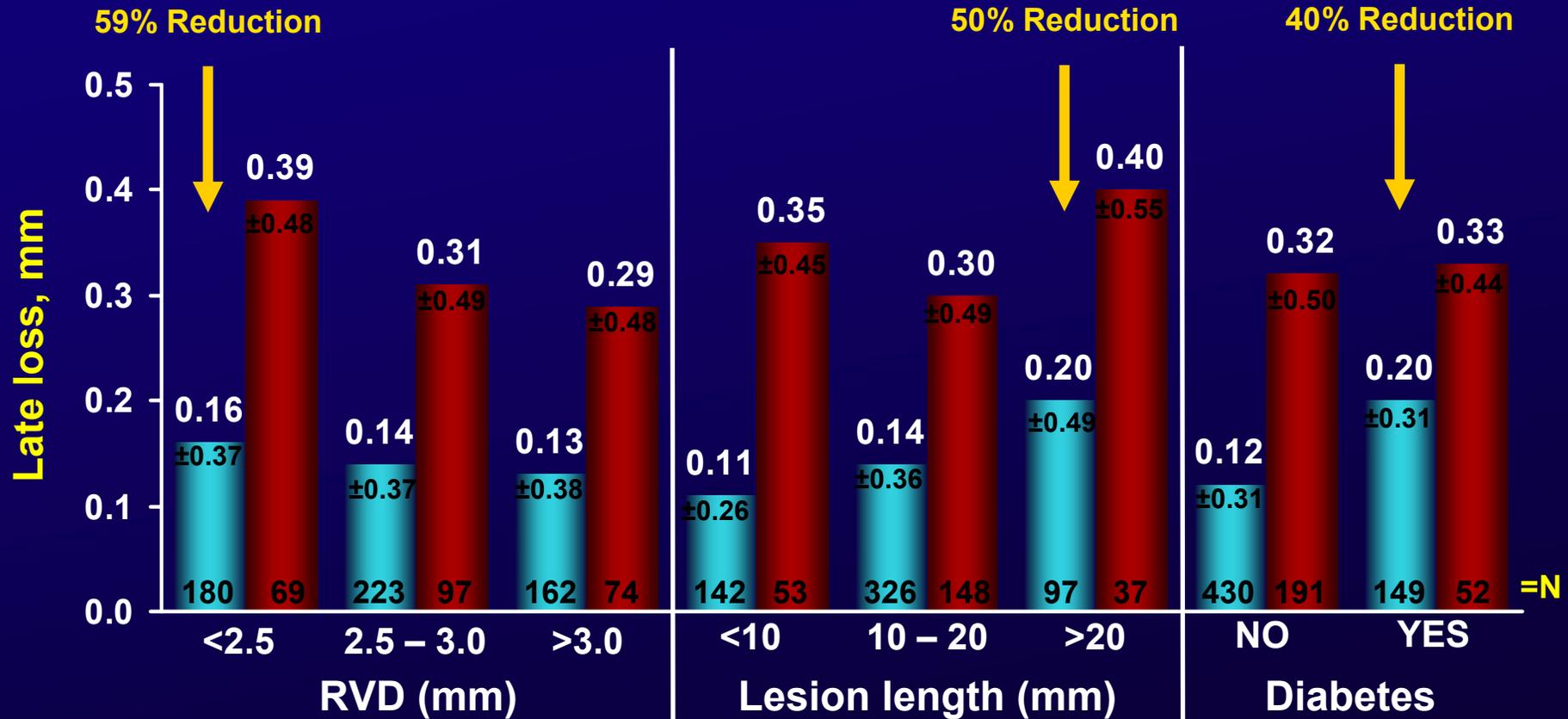
Number at Risk

XIENCE V	892	867	851	821	806
TAXUS	409	385	381	361	353

SPIRIT II & III Pooled Analysis

Pre-Specified Subgroups: In-stent LL

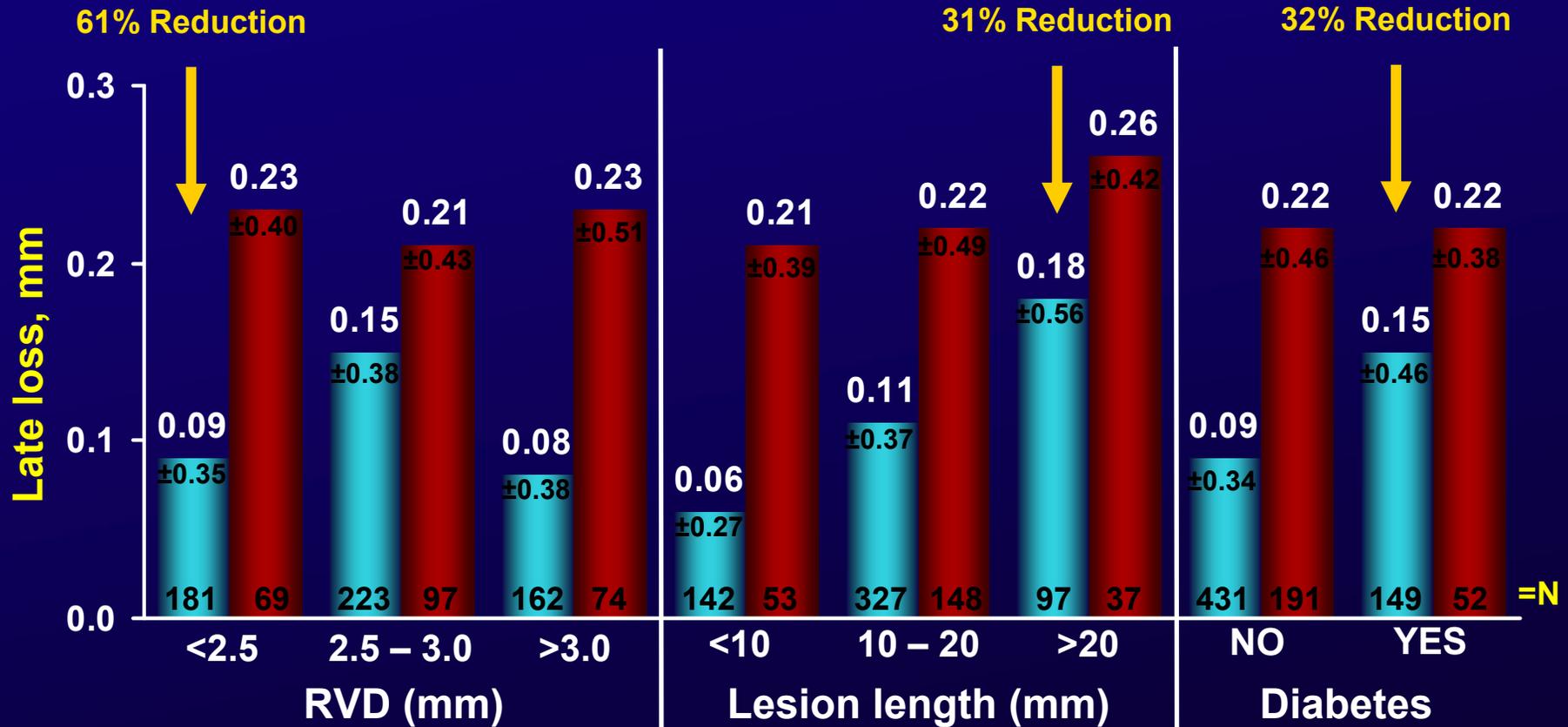
■ XIENCE V ■ TAXUS



SPIRIT II & III Pooled Analysis

Pre-Specified Subgroups: In-segment LL

■ XIENCE V ■ TAXUS



Perspectives from the “New DES” vs. TAXUS RCTs

Study	Stent	In-stent LL	In-seg LL	In-seg ABR	TLR	TVR	MACE	TVF
Zomaxx I ¹	Zomaxx vs. TAXUS	↑ 49%	↑ 80%	↑ 140%	↑ 95%	↑ 129%	↑ 31%	↑ 43%
Costar II ²	Costar vs. TAXUS	↑ 67%	↑ 200%	↑ 152%	↑ 113%	↑ 188%	↑ 60%	–
Endeavor IV ³	Endeavor vs. TAXUS	↑ 60%	↑ 57%	↑ 47%	↑ 41%	↑ 6%	↓ 2%	↓ 8%
SPIRIT III ⁴	XIENCE V vs. TAXUS	↓ 48%	↓ 50%	↓ 47%	↓ 46%	↓ 29%	↓ 43%	↓ 22%

1) Zomaxx I trial results are on file with sponsor, Abbott Vascular

2) Costar II; EUROSTAR II Trial presented by M. Krucoff at PCR 2007

3) Endeavor IV results presented by M. Leon at TCT 2007

4) Clinical event rates for XIENCE V calculated from 284 day data

XIENCE V Stent: Conclusions from Clinical Studies

- With follow-up complete through 1 year, the XIENCE V everolimus-eluting stent compared to the TAXUS paclitaxel-eluting stent results in:
 - **Significant reductions** in angiographic in-stent and in-segment late loss and binary restenosis
 - **Significant reduction** in IVUS percent volume obstruction ,without positive remodeling or late acquired incomplete apposition
 - **Significant reductions** in MI, MACE and TVF at 30 days, with **non significant numerical trends** toward less composite cardiac death and MI, and TVF at 1 year
 - **Significant reductions** in TLR and MACE at 1 year
 - **Comparable** rates of stent thrombosis

XIENCE V Stent: Conclusions from Clinical Studies

- The clinical and angiographic benefits of the everolimus-eluting XIENCE V stent compared to the widely utilized paclitaxel-eluting TAXUS stent have been consistent in 2 consecutive randomized trials in 2 different geographies; as such, these findings may be considered especially robust
- Every pre-specified primary and major secondary endpoint from the SPIRIT FIRST randomized trial, the SPIRIT II randomized trial, and the SPIRIT III randomized trial were successfully met

XIENCE V

Safety Considerations

Mitchell W. Krucoff MD

Professor of Medicine / Cardiology
Duke University Medical Center
Director, Cardiovascular Devices Unit
Duke Clinical Research Institute



Conflict of Interest

- No equity holding or significant conflict
- Consulting* and/or research grants from the following:
 - Cordis J&J
 - Medtronic
 - Boston Scientific
 - Biosensors
 - Affinergy
 - Abbott
 - St. Jude Medical
 - OrbusNeich
 - Conor
 - Terumo

* Moderate: < \$10,001 per annum

Reasonable Assurance of XIENCE V Safety: Presentation Overview

- Prospective study analyses: safety context
- 2 year safety subset
- Continued Access/Post-approval Program

Safety Context for 1 Year Pooled SPIRIT II & III Analysis

Consistency Across The Spectrum of Prospective Safety & Effectiveness

XIENCE V vs. TAXUS

Study	In-stent LL	In-seg LL	In-stent ABR	In-seg ABR	TLR @ 1 yr	MACE @ 1 yr	TVF @ 1 yr
SPIRIT II	↓ 69%	↓ 53%	↓ 63%	↓ 41%	↓ 73%	↓ 71%	↓ 51%
SPIRIT III	↓ 47%	↓ 50%	↓ 60%	↓ 47%	↓ 39%	↓ 42%	↓ 24%
SPIRIT II and III Pooled	↓ 58%	↓ 50%	↓ 61%	↓ 47%	↓ 47%	↓ 48%	↓ 29%

Late Stent Thrombosis & DES Safety

- Contemporary focus: Fall 2006 (ESC)
- Rare events: $\leq 0.6\%$ per annum
- Complex substrate issue:
 - Patient
 - Procedure
 - Platform
 - Plavix
- Statistical certainty:
 - Large patient cohorts
 - Long term follow up

BMS vs. DES - Meta Analyses

Stent thrombosis 4 years

Kastrati A, et al. Eur Heart J. Sep 27; Epub ahead of print.

Brunner La-Rocha H, et al. Eur Heart J. 2007 Mar;28(6):719-25.

Lagerqvist B et al. N Engl J Med. 2007 Mar 8;356(10):1009-19.

Stettler C, et al. Lancet 2007 Sep 15;370(9591):937-48.

Ellis S, et al. Am Coll Cardiol 2007 Mar 13;49(10):1043-51.

Moreno R, et al. Am J Cardiol 2007 Mar 1;99(5):621-5.



Over 15 meta-analyses comparing DES to BMS

Dibra A, et al. J Am Coll Cardiol 2007 Feb 6;49(5):616-23.

Holmes D, et al. Eur Heart J 2006;27(23):2815-22.

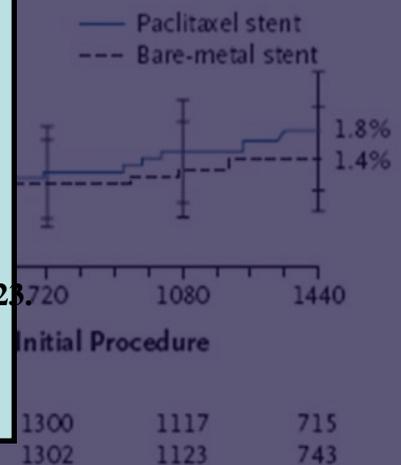
Nordmann A, et al. Eur Heart J 2006;27(23):2784-814.

Moses J, et al. J Am Coll Cardiol. 2006 Jun 6;47(11):2164-71.

Moreno R, et al. J Am Coll Cardiol. 2005 Mar 15;45(6):954-9.

Biondi-Zoccai G., et al. Intl J of Cardiol 2005 Apr 8;100(1):119-23.

Babapulle M, et al. Lancet 2004;364(9434):558-9.



Initial Procedure	Paclitaxel stent	Bare-metal stent
1300	1117	715
1302	1123	743
Bare-metal stent	1397	1353

Overall rates of stent thrombosis (per protocol) not significantly different for paclitaxel DES vs. BMS 4 years follow

Mauri, L. et al. (2007), NEJM; 356:1020-29

Special FDA Panel on DES Thrombosis December 2006

When used for the approved indications,

sa
be

**On label use of TAXUS
DES is safe and effective
relative to BMS**

“C
w
fo

evident increase in the rates of mortality or
myocardial infarction”

Maisel, B. (2007). NEJM, 356:10(981-84)

panel

ed
ed

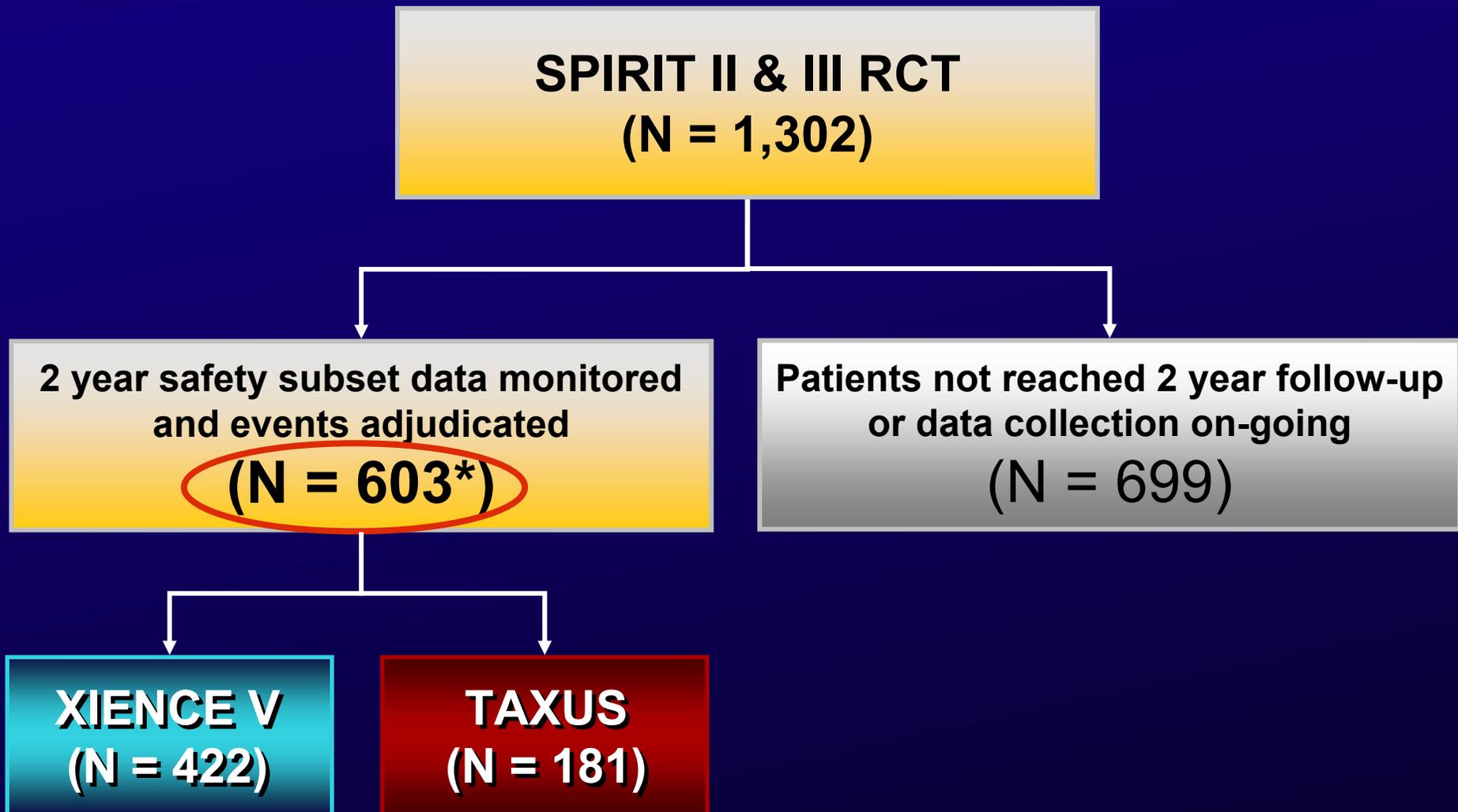
2 Year Pooled Spirit II & III Safety Subset

New DES vs. Approved DES

SPIRIT II & III Pooled Analysis: 2 Year Safety Subset

- 2 year Safety Data analysis
 - Not a prospective analysis plan for either SPIRIT II or SPIRIT III
 - Statistical Analysis Plan (SAP) developed based on discussions with FDA
 - 2 year safety subset subjects “inclusion” criterias specified in the SAP:
 - Subjects must have completed 2 year follow-up by or must have terminated prior to Oct. 30, 2007 (e.g. “all available” as of Oct 30, 2007)
 - All data must be monitored (100% source verification)
 - All events must be adjudicated by independent blinded CECs

SPIRIT II & III 2 Year Safety Subset: Clinical Follow-up Patient Flow



* Include 74 early terminators (Patients died = 30, LTFU = 29, or withdrew = 15)

SPIRIT II & III Pooled Analysis

Early Terminators in 2 Year Safety Subset

- Among the 74 monitored early terminators:
 - 43 terminated before 1 year
 - 31 terminated between year 1 and 2
 - The range of denominators for 0-2 year analysis is 534 - 563

SPIRIT II & III Pooled 2 Year Analysis

Baseline Characteristics

	Complete Cohort		2 Year Subset	
	XIENCE V	TAXUS	XIENCE V	TAXUS
	n = 892 pts	n = 410 pts	n = 422 pts	n = 181 pts
Age (mean) (years)	62.9	62.6	62.8	62.8
Male (%)	70.3	68.2	70.4	68.5
Diabetes (%)	27.9	27.1	26.1	25.7
Hypertension (%)	74.0	72.3	69.9	68.9
Hypercholesterolemia (%)	72.8	72.1	70.0	70.1
Current Smoker (%)	25.3	23.8	25.1	27.4
Prior MI (%)	23.7	19.3	27.1	22.1
Unstable Angina (%)	20.8	26.5	24.8	26.7
Dual vessel treatment (%)	15.7	15.9	17.1	16.6

SPIRIT II & III Pooled 2 Year Analysis

Angiographic Characteristics

	Complete Cohort		2 Year Subset	
	XIENCE V	TAXUS	XIENCE V	TAXUS
	n = 1,032 lesions	n = 474 lesions	n = 494 lesions	n = 211 lesions
LAD (%)	41.1	43.8	40.5	44.1
LCX (%)	28.0	26.4	28.3	25.1
RCA (%)	30.7	29.6	31.2	30.3
LMCA (%)	0.1	0.2	0.0	0.5
RVD (mean) (mm)	2.75	2.77	2.72	2.76
MLD (mean) (mm)	0.88	0.89	0.91	0.92
%DS (mean)	67.7	67.5	66.2	66.2
Lesion Length (mean) (mm)	14.3	14.5	14.3	14.7

SPIRIT II & III Pooled 2 Year Analysis

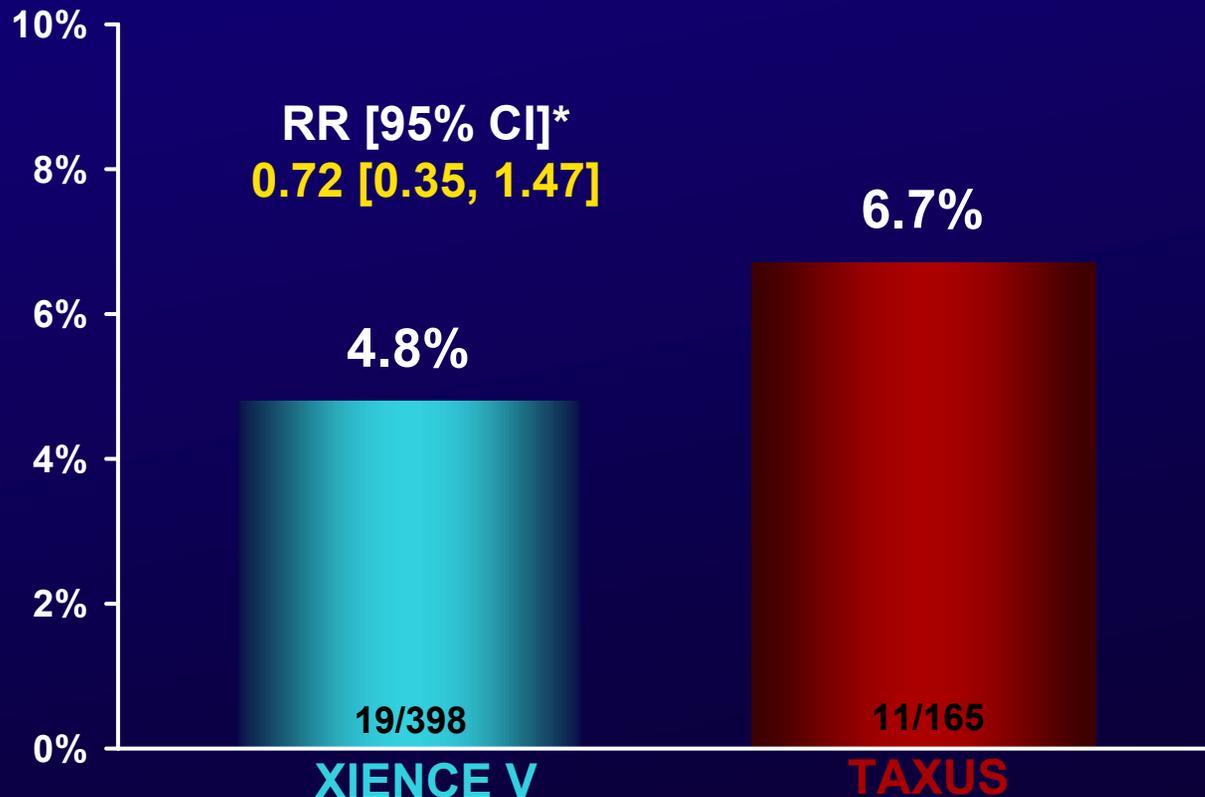
Antiplatelet Agent Utilization

	Complete Cohort		2 Year Completers*	
	XIENCE V	TAXUS	XIENCE V	TAXUS
	n=892 pts	n=410 pts	n=377 pts	n=153 pts
Aspirin				
At 6 months (%)	97.3	95.8	98.7	94.8
At 9 months (%)	96.5	94.6	98.1	94.8
At 1 year (%)	95.4	92.9	97.6	94.1
At 2 years (%)	—	—	96.3	94.1
Thienopyridine				
At 6 months (%)	93.4	92.9	91.8	94.8
At 9 months (%)	67.8	70.6	58.6	66.0
At 1 year (%)	63.3	64.5	52.5	58.8
At 2 years (%)	—	—	40.6	49.0

* Excluding early terminators

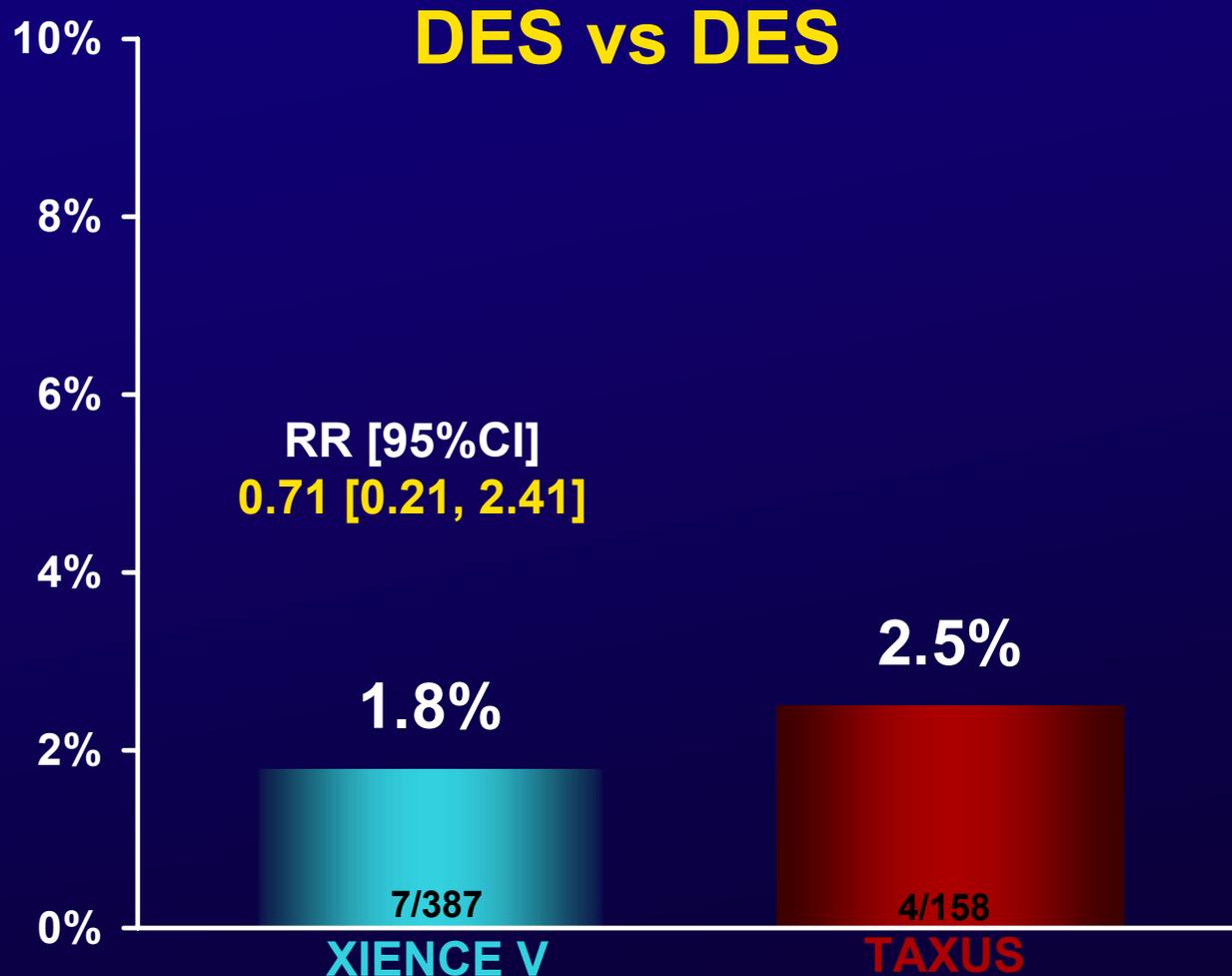
SPIRIT II & III 2 Year Safety Subset: All Death

DES vs DES

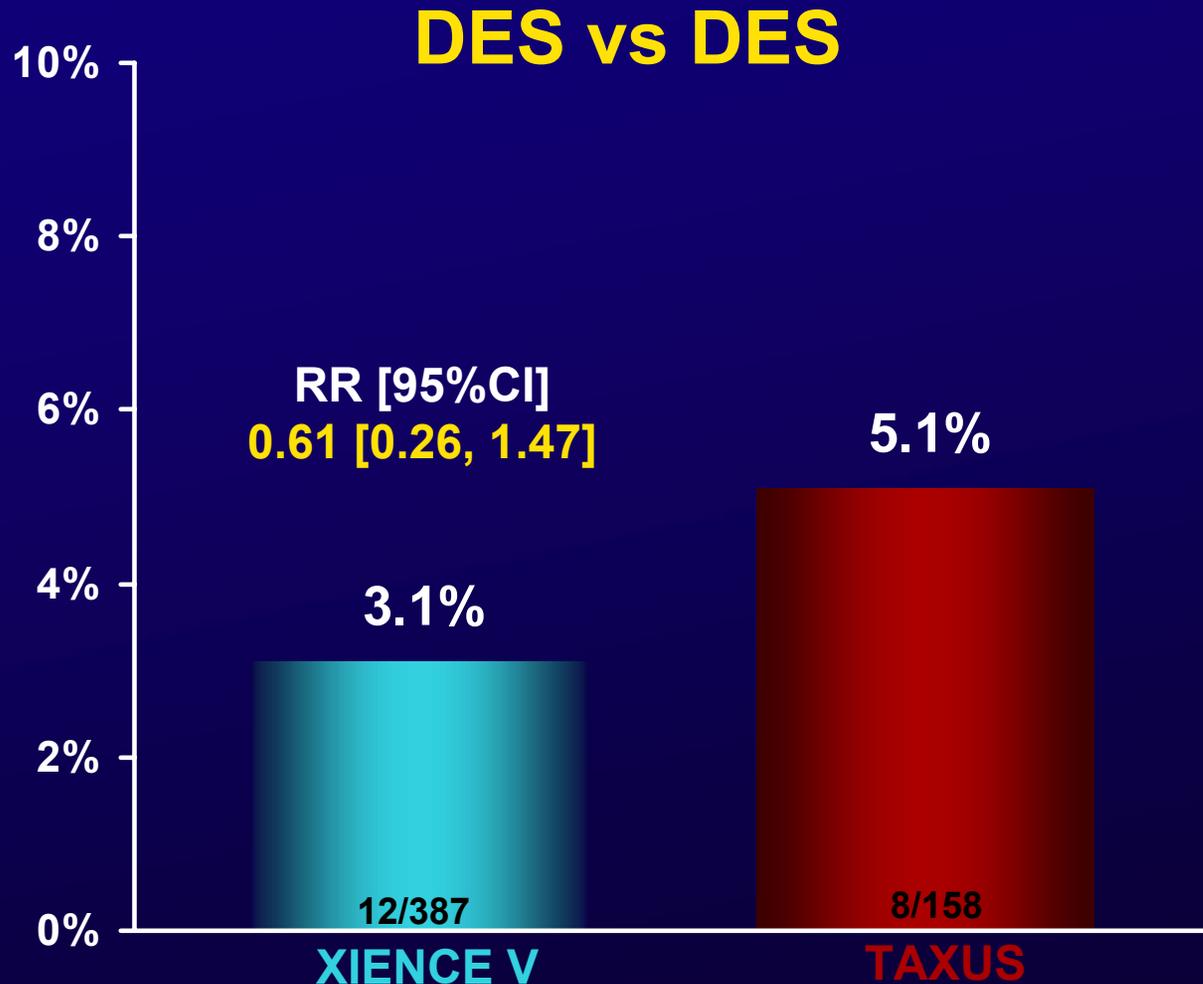


* Confidence Intervals are for descriptive purposes only and not adjusted for multiple comparisons

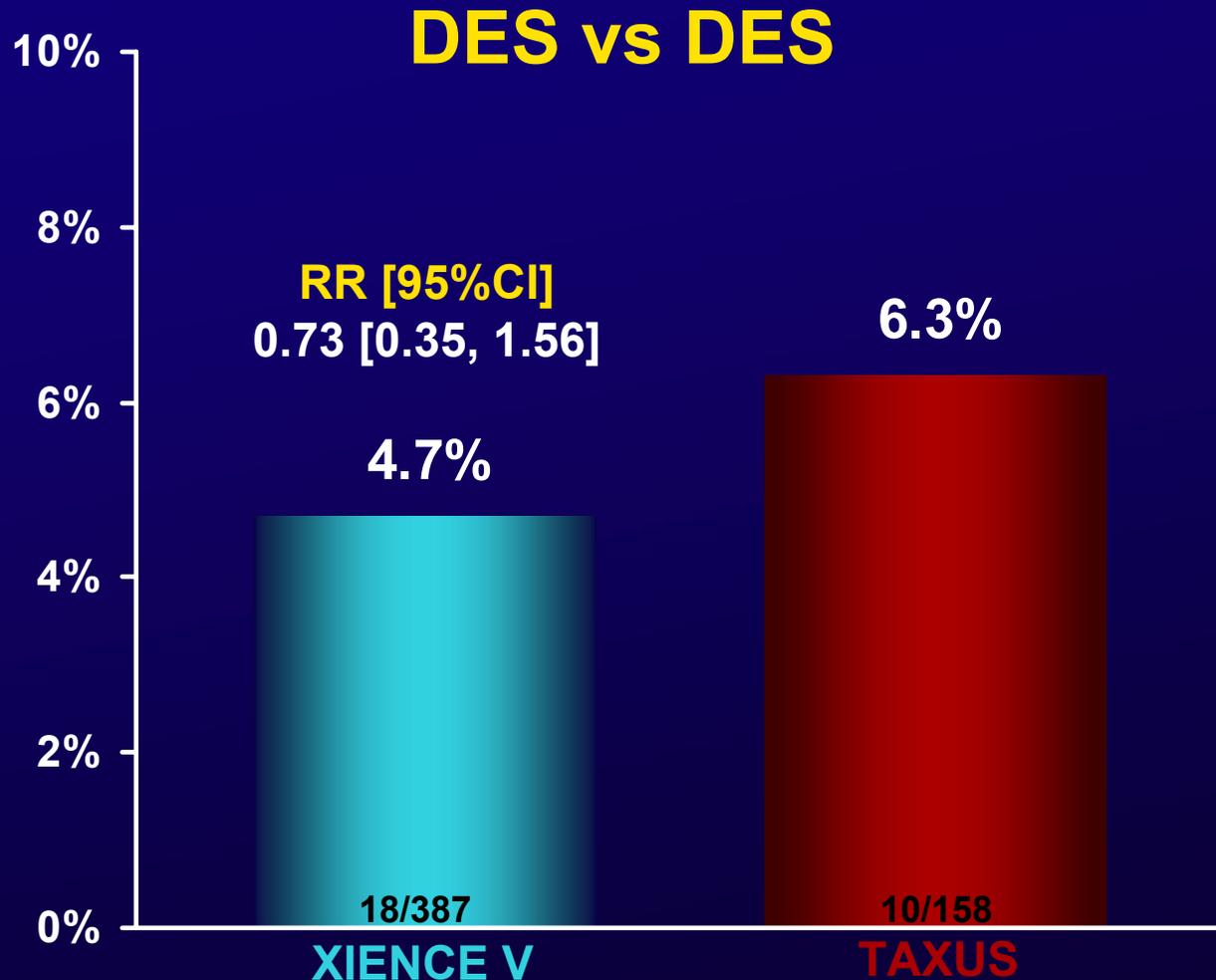
SPIRIT II & III 2 Year Safety Subset: Cardiac Death



SPIRIT II & III 2 Year Safety Subset: MI

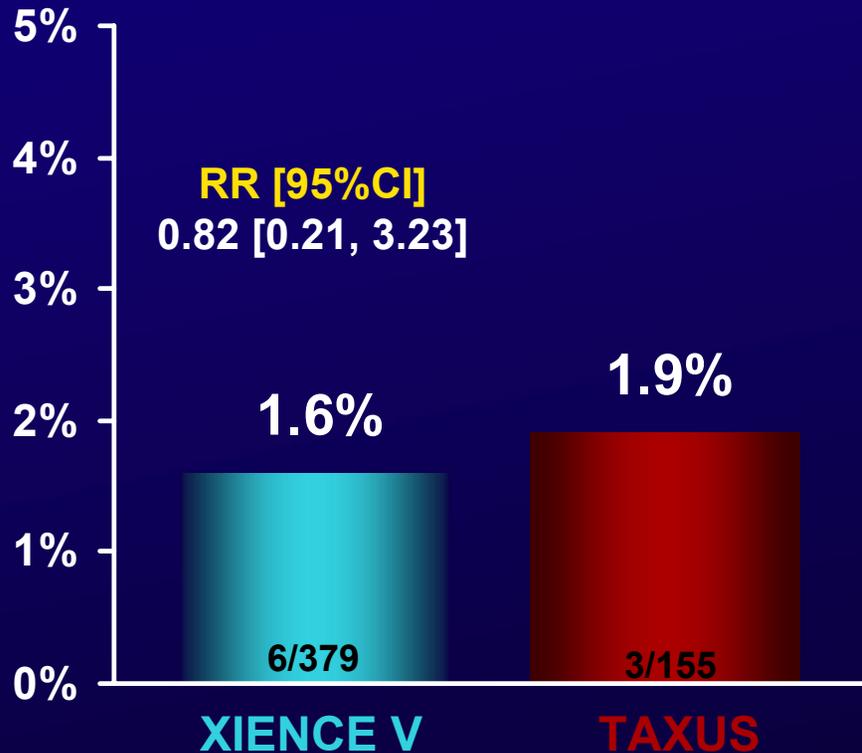


SPIRIT II & III 2 Year Safety Subset: Cardiac Death or MI

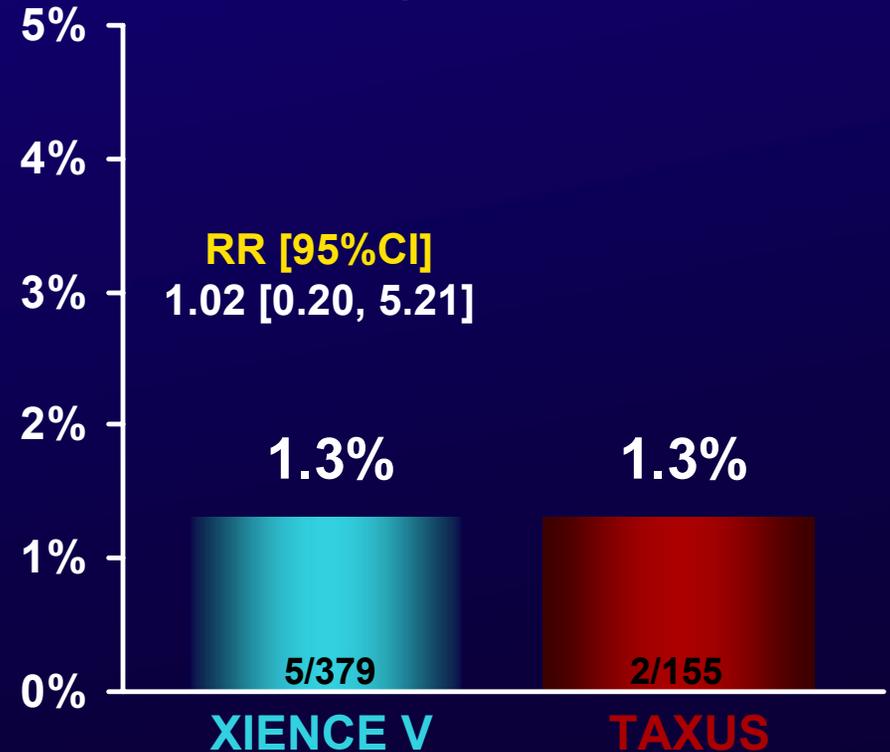


SPIRIT II & III 2 Year Safety Subset: Stent Thrombosis

Stent Thrombosis Per Protocol



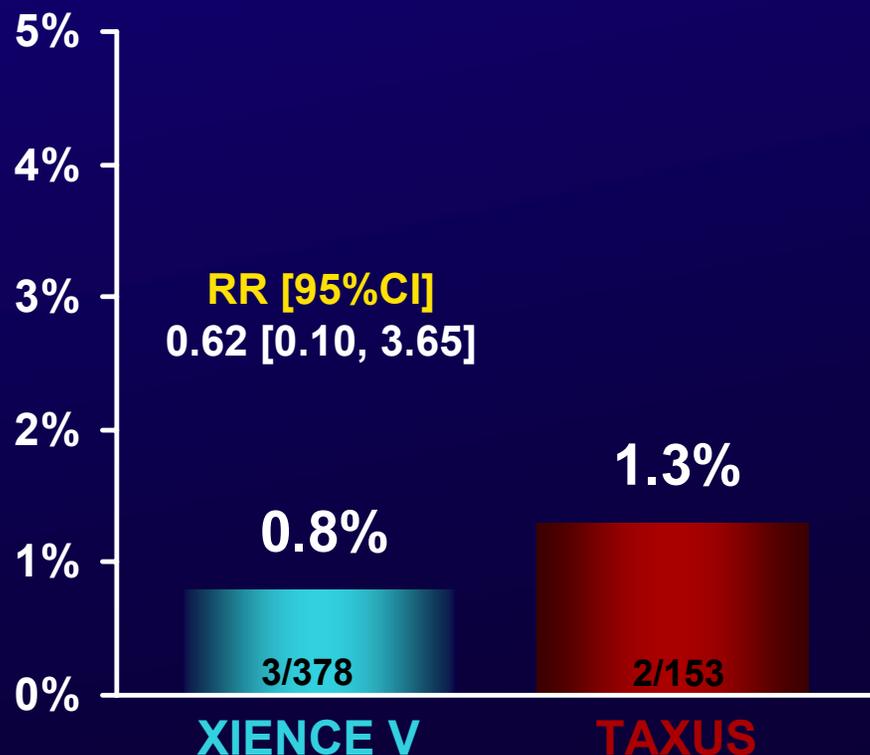
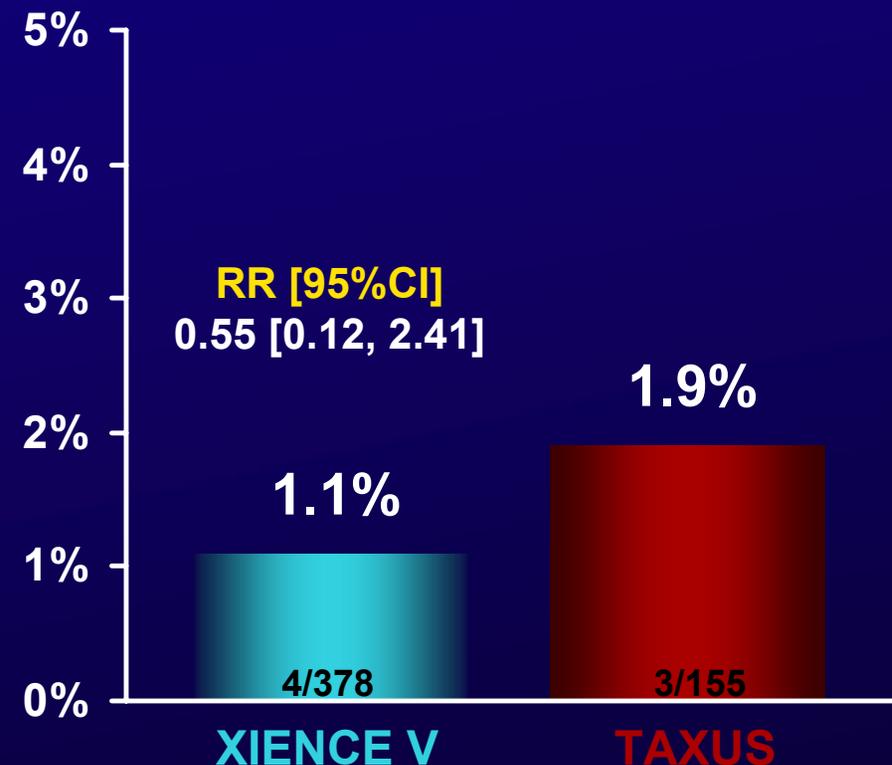
Stent Thrombosis Per ARC (Definite + Probable)



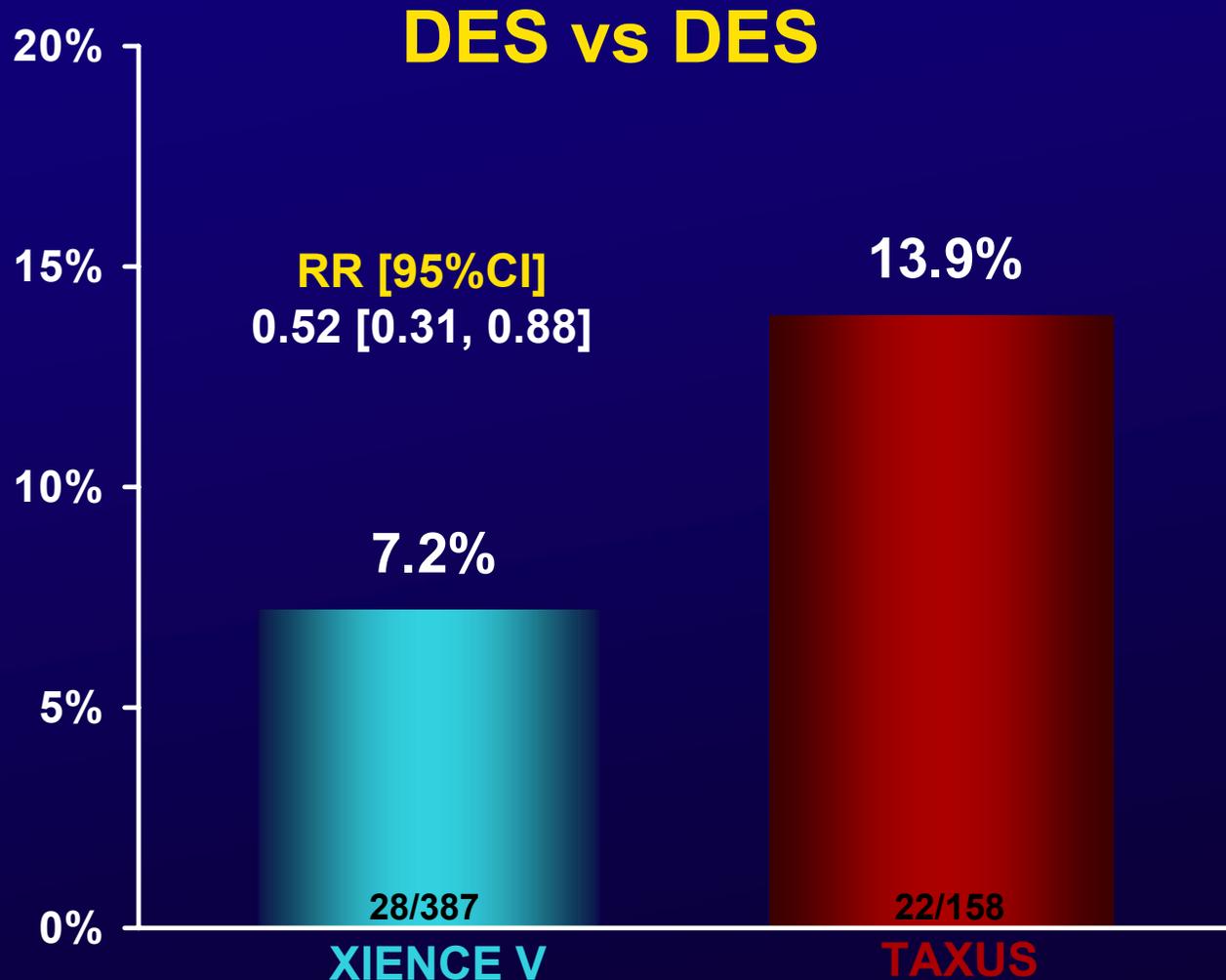
SPIRIT II & III 2 Year Safety Subset: Late/Very Late Stent Thrombosis (31 days – 2 yrs)

Per Protocol

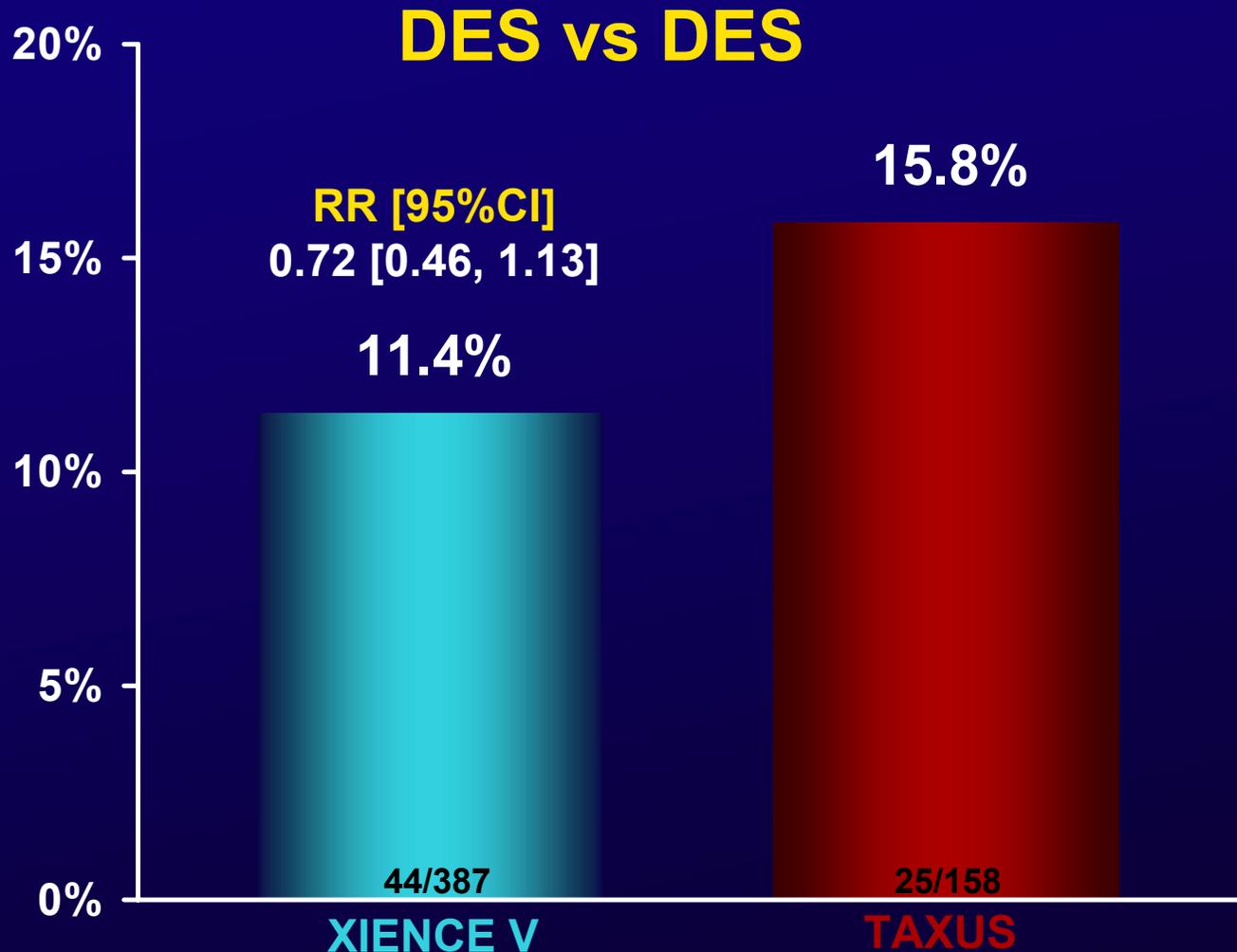
Per ARC (Definite + Probable)



SPIRIT II & III 2 Year Safety Subset: MACE



SPIRIT II & III 2 Year Safety Subset: TVF



SPIRIT II & III

Pooled Analysis: Observations

- 2 year Safety Subset Analysis from SPIRIT II and SPIRIT III shows:
 - Similar baseline and angiographic data compared to the total cohort
 - Slightly lower long term clopidogrel use (≥ 9 Months) in the safety subset compared to the entire study population
 - Directionality of endpoints at 2 years in safety subset consistent with outcomes at 1 year in entire cohort
 - No evidence of any safety signal at 2 years based on all available monitored data

XIENCE V Safety: Reasonable Assurance of Safety

- Design objectives met or exceeded:
 - Second generation stent platform
 - Advanced polymer design
 - Well characterized drug entity
 - Preclinical models through 2 years
- Human trials:
 - Non inferior or superior in all prospective angiographic and clinical safety and efficacy endpoints at one year
 - Two year directionality of safety endpoints very consistent with 1 year
 - No evidence for safety concerns apparent compared to TAXUS based on all available monitored data at 2 year follow-up

Sample Size for Rare Endpoints

Assumed Rate (per year)	0.3%	0.4%	0.5%
Delta (RR = 1.5)	0.15%	0.2%	0.25%
80% Power* Alpha = 0.025	11,926	8,944	7,156
90% Power* Alpha = 0.025	16,610	12,458	9,966

* Sample size determined using NCSS PASS using Post Market Surveillance

XIENCE V
Continued Access/Post
Approval Program

Integrated Pre-Approval and Post-Approval Clinical Program (N > 16,000)

Pre-approval Clinical Data

SPIRIT First

RCT 1:1 XIENCE V vs. VISION (n = 60) OUS

SPIRIT II

RCT 3:1 XIENCE V vs. TAXUS (n = 300) OUS

SPIRIT III

RCT 2:1 XIENCE V vs. TAXUS (n = 1,002) US

SPIRIT III 4.0

Registry 4.0 mm (n = 80) US

Ongoing and Planned Clinical Data

SPIRIT III Japan

Registry (n = 88) Japan

SPIRIT IV

RCT XIENCE V vs. TAXUS 2:1 Continued Access (n = 3,690) US

SPIRIT V

Registry (n = 2,700), RCT Diabetics 2:1 vs. TAXUS (n = 300) OUS

**XIENCE V
SPIRIT Women**

Registry (n = 1,550) RCT 2:1 vs. CYPHER (n = 450) OUS

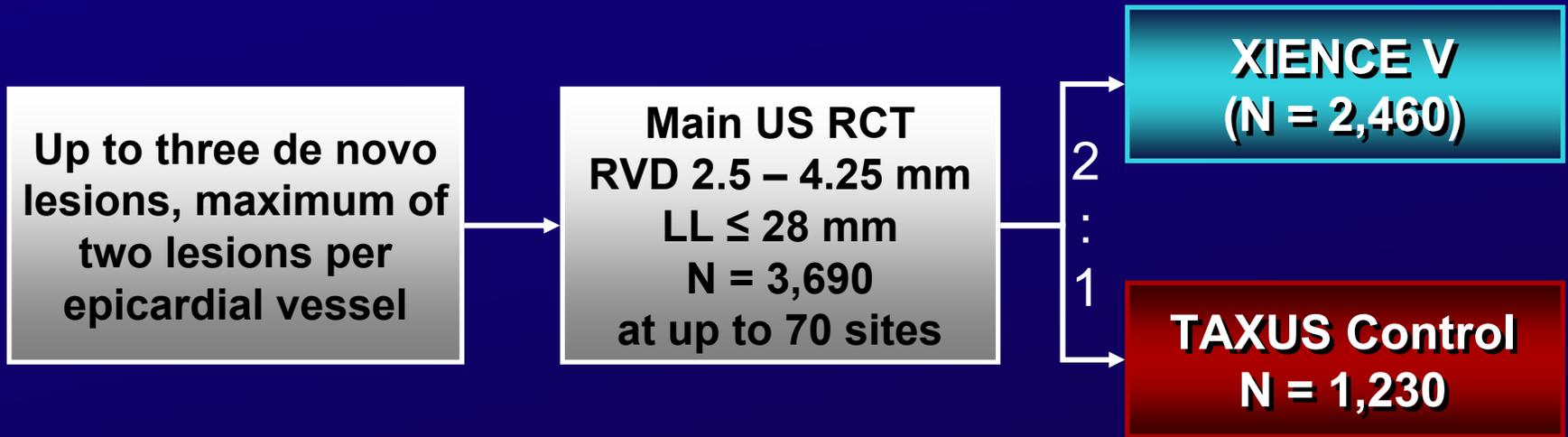
XIENCE V USA

Post-approval Registry – real world (n ~ 5,000) US

XIENCE India

Post-approval Registry – real world (n ~ 1,000) OUS

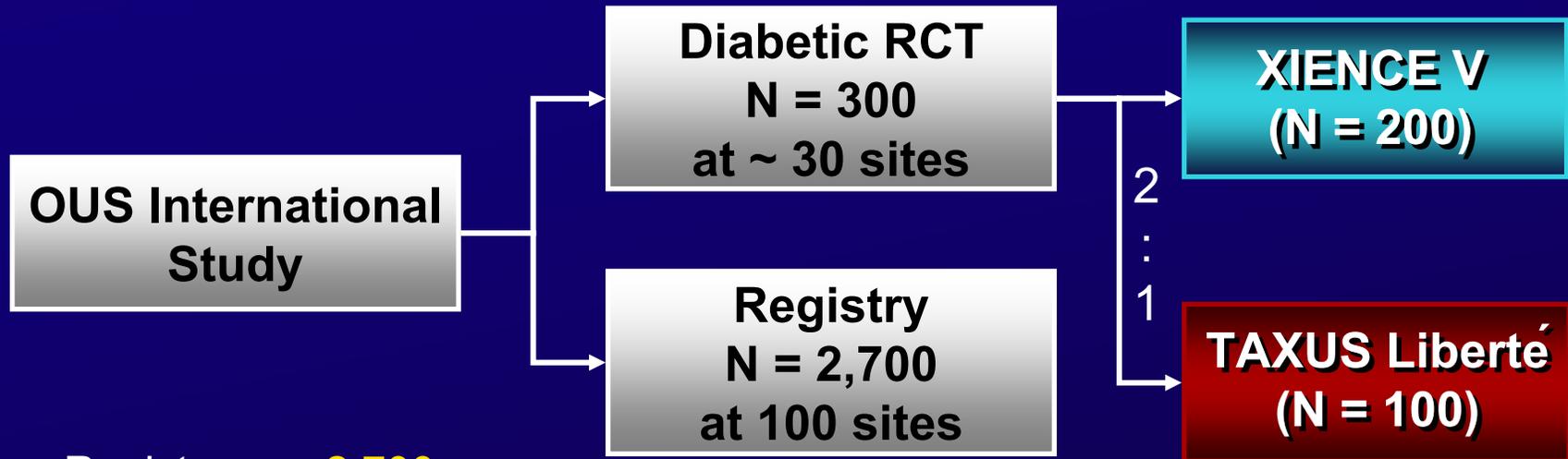
SPIRIT IV



- Prospective, single blind, randomized, continued access trial in 3,690 patients
- Expanded multi-vessel treatment
- Primary endpoint: MACE at 1 year*
- Clinical follow-up to 5 years
- Currently enrolling (2,225 patients enrolled by November 26, '07)
- 3 DSMB meetings – No safety-related issues reported to date
- PI: Gregg Stone

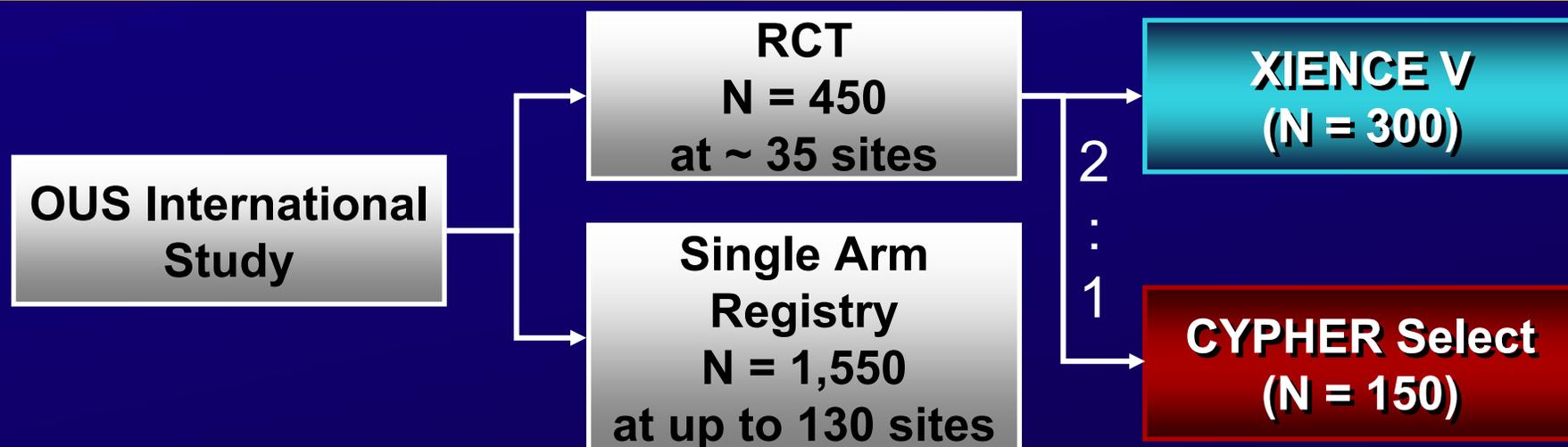
* Under discussions with FDA

SPIRIT V



- Registry: $n = 2,700$
 - Primary endpoint: adjudicated composite rate of death, MI and TVR at 30 days
 - Clinical follow-up to 5 years
- Diabetic study: $n = 300$
 - Primary endpoint: In-stent LL at 270 d, compared to TAXUS, 2:1
 - Angiographic follow up at 9 months, clinical follow-up to 5 years
- Enrollment complete in registry, 2,700 patients enrolled
- 3 DSMB meetings – no safety related issues reported to-date
- PI: Eberhard Grube, MD

SPIRIT Women



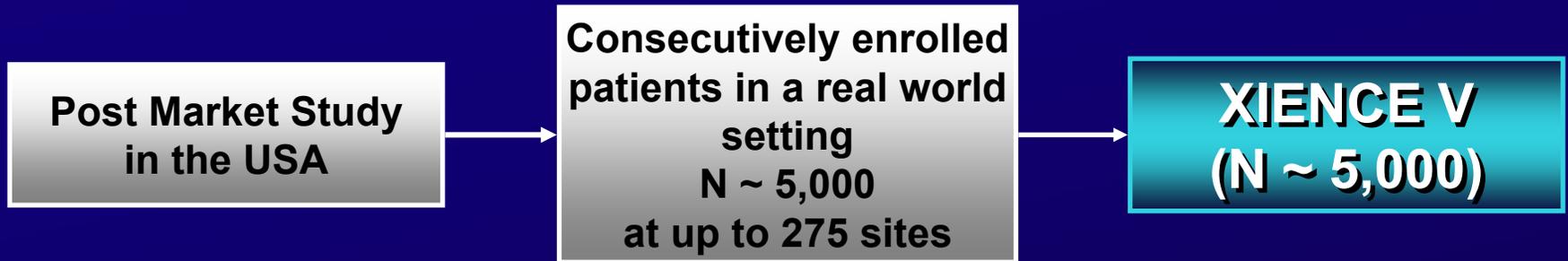
- Single Arm Registry: **n = 1,550**
 - Primary endpoint: Composite rate of all Death, all MI & TVR at 1 year
 - Clinical follow-up to 5 years
- RCT: **n = 450** vs. CYPHER, 2:1
 - Primary endpoint: Composite rate of all Death, all MI & TVR at 1 year
 - Clinical follow-up to 5 years
 - Angiographic follow-up at 9 months
- Currently enrolling (enrollment commenced July 2007)
- PI: Marie-Claude Morice, MD Co-PI: Stephan Windecker, MD

XIENCE V India



- Post market registry in ~ 1,000 real world patients
- Primary endpoint: ARC defined stent thrombosis through 5 years
- Co-primary endpoint: Composite endpoint of death and MI at 1 year and through 5 years
- Clinical follow-up to 5 years
- Procedural success during commercial use
- Health status by the Seattle Angina Questionnaire
- Patient compliance with adjunctive antiplatelet therapy and major bleeding complications
- PI: Ashok Seth, MD

XIENCE V USA

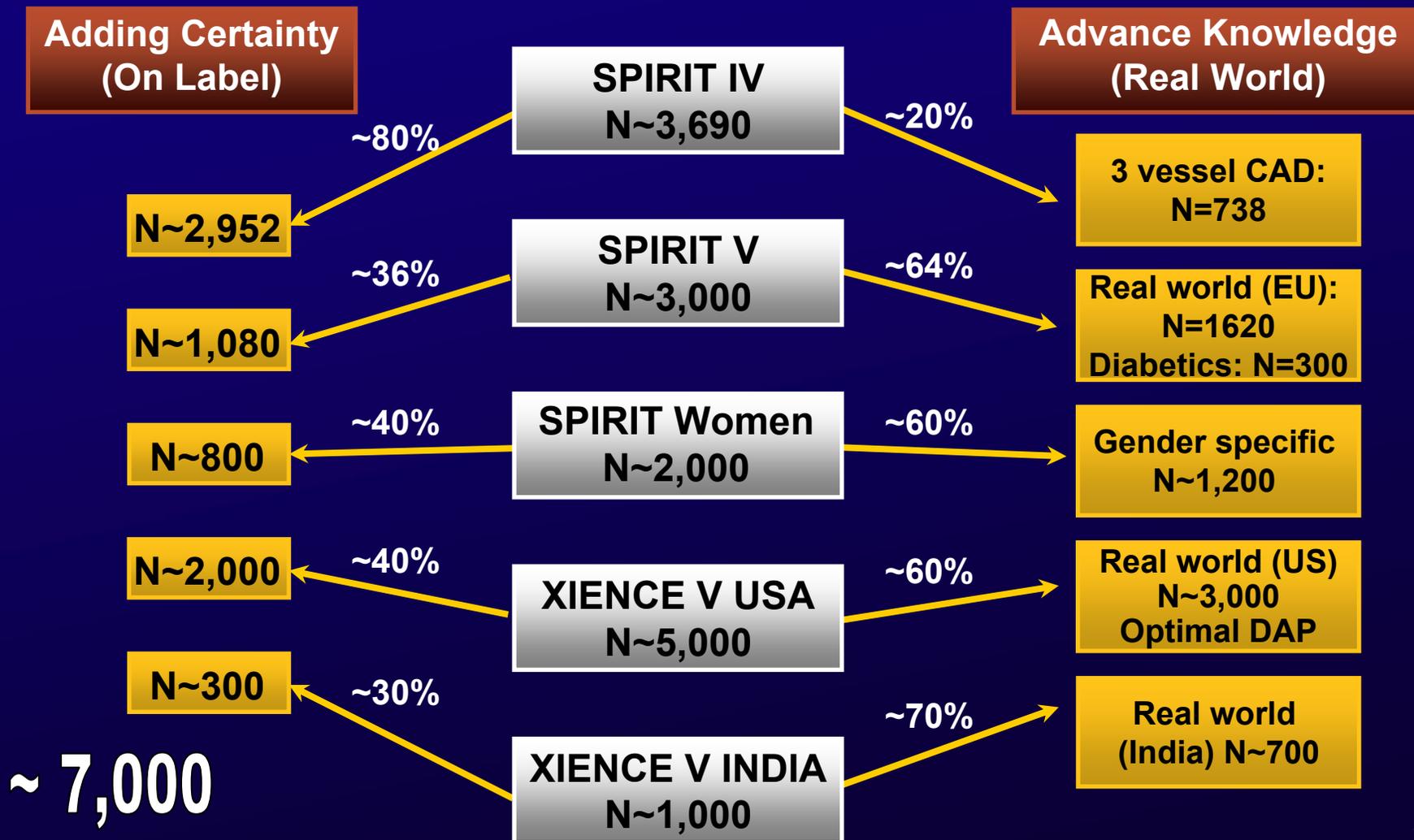


- Post-approval registry in ~ 5,000 real world patients
- Primary Endpoint: ARC defined stent thrombosis through 5 years
- Secondary Endpoint: Composite death and MI at 1 year and through 5 years
- Procedural success during commercial use
- Health status by the Seattle Angina Questionnaire
- Evaluate compliance with adjunctive antiplatelet therapy, management of interruption and major bleeding complications
- Abbott Vascular Considerations:
 - Composite Death and MI as co-primary
 - Optimal dual anti-platelet therapy duration
- Co-PI's: James Hermiller, MD & Mitchell Krucoff, MD

SPIRIT/XIENCE V

Integrated Post-Approval Strategy

Post-Approval Trials N=14,690; (Randomized: 4,440)



XIENCE V Continued Access/Post Approval Program: Conclusions

- Evaluates continued safety and performance over 5 years
 - ~ 14,690 patients worldwide
 - ~ 8,600 patients in US
 - ~ 4,900 already enrolled (without DSMB modifications)
- Integrated, committed post approval program utilizing systematic, high quality science delivered from post-market research landscape
- Will prospectively provide additional statistical certainty about on-label XIENCE V safety
- Will prospectively provide new knowledge regarding off-label and real world XIENCE V use

Conclusions

Krishna Sudhir, MD, PhD

XIENCE V Design

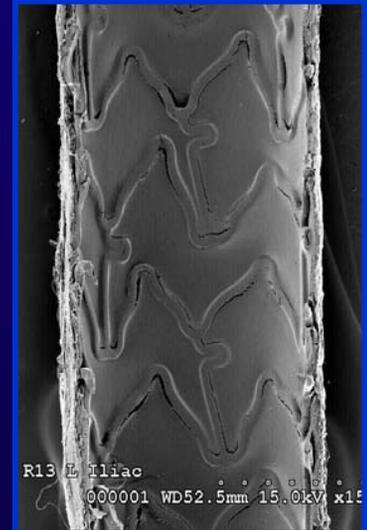
- Built on the well established ML VISION and MINI-VISION Stent and Stent Delivery System
 - Flexible stent with thin struts
 - Proven deliverability
- Thin, biocompatible drug coating
 - Durable polymer, used in other Cardiovascular applications
 - Long term biocompatibility similar to VISION BMS
- Well studied drug, not a new molecular entity



Pre-clinical Program

- Comprehensive pre-clinical evaluation with 35 studies, 2 species, 28 days to 2 years
- Rapid re-endothelialization
- Smooth muscle cell rich neointima
 - No persistent fibrin
 - Minimal long term inflammation
- Hemocompatibility comparable to VISION BMS
- Pre-clinical safety profile equivalent to VISION BMS

XIENCE V



Integrated Pre-Approval and Post-Approval Clinical Program (N > 16,000)

Pre-approval Clinical Data

SPIRIT First

RCT 1:1 XIENCE V vs. VISION (n = 60) OUS

SPIRIT II

RCT 3:1 XIENCE V vs. TAXUS (n = 300) OUS

SPIRIT III

RCT 2:1 XIENCE V vs. TAXUS (n = 1,002) US

SPIRIT III 4.0

Registry 4.0 mm (n = 80) US

Ongoing and Planned Clinical Data

SPIRIT III Japan

Registry (n = 88) Japan

SPIRIT IV

RCT XIENCE V vs. TAXUS 2:1 Continued Access (n = 3,690) US

SPIRIT V

Registry (n = 2,700), RCT Diabetics 2:1 vs. TAXUS (n = 300) OUS

**XIENCE V
SPIRIT Women**

Registry (n = 1,550) RCT 2:1 vs. CYPHER (n = 450) OUS

XIENCE V USA

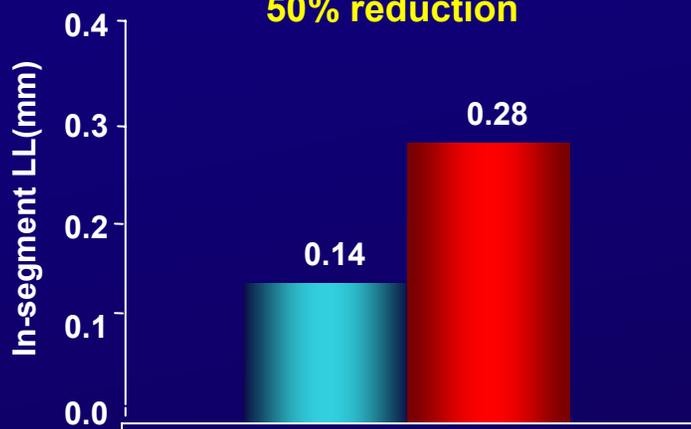
Post-approval Registry – real world (n ~ 5,000) US

XIENCE India

Post-approval Registry – real world (n ~ 1,000) OUS

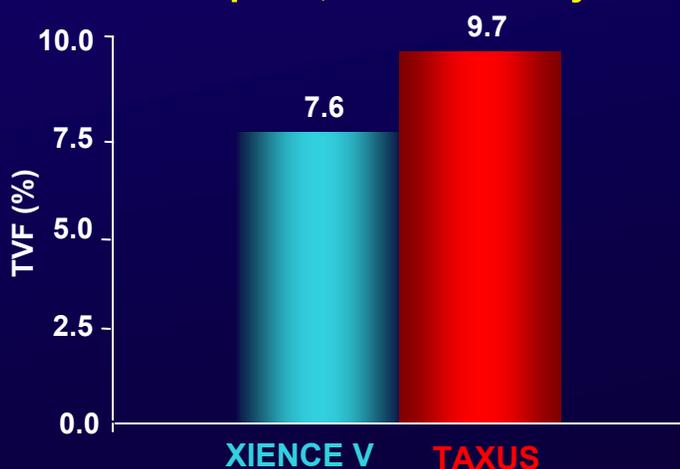
Robust Evidence of Effectiveness

**SPIRIT III: Primary Endpoint,
50% reduction**



Consistent clinical and angiographic benefits of the XIENCE V stent compared to TAXUS, in 2 consecutive randomized trials (SPIRIT II and III) in multiple geographies

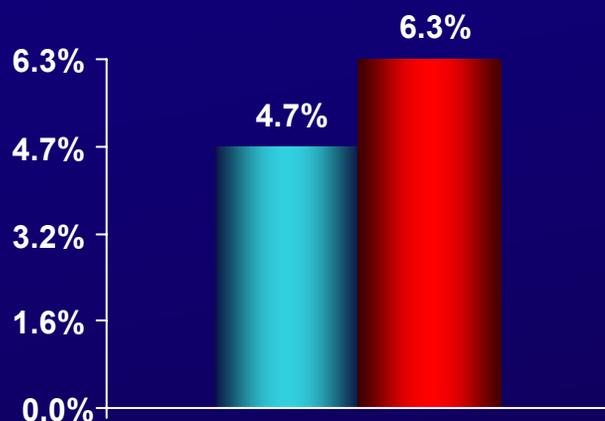
**SPIRIT III: Secondary
Endpoint, non-inferiority**



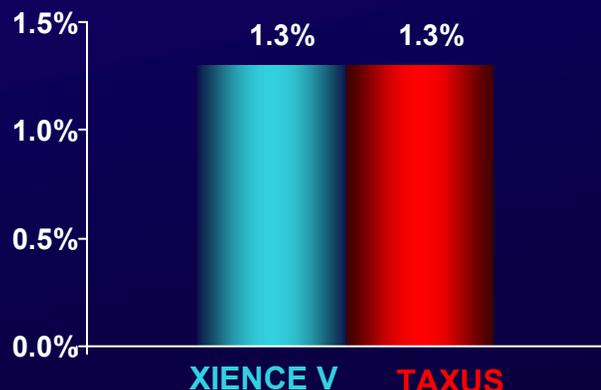
All pre-specified primary and major secondary endpoints from the SPIRIT FIRST randomized, SPIRIT II randomized, SPIRIT III randomized trials were successfully met

Reasonable Assurance of Safety

2-yr safety subset:
Cardiac Death or MI



Stent Thrombosis Per ARC
(Definite + Probable)



XIENCE V demonstrates reasonable assurance of safety, with comparable 1 year death, MI and Stent thrombosis rates to TAXUS

No differences apparent in safety events at 2 years between treatment groups based on all available monitored data

Thus, no safety concerns apparent as compared to TAXUS based on all available data to date

Summary

- Clinical results consistent with design intent and pre-clinical observations
- SPIRIT FIRST, II and III all met their primary and major secondary endpoints; SII and SIII results confirmed in pooled analysis
- Superiority in angiographic endpoint (Late Loss), and non-inferiority in clinical endpoint (Target Vessel Failure), compared to TAXUS
- Reasonable assurance of safety as demonstrated by similar rates of Death, MI and Stent Thrombosis compared to TAXUS up to 2 years.

Post-Approval Considerations

- In post-market surveillance programs, sample sizes for low frequency events ($< 0.5\%$ per year) can vary from $\sim 7,000 - 16,000$ patients
- Abbott Vascular has a comprehensive, integrated pre-approval and post-approval plan with $> 16,000$ patients, and five year follow-up
- A robust post-approval program with 14,690 patients worldwide and 5 year follow-up has been presented today, designed to detect the true incidence of low frequency adverse events