Absorb GT1™ Bioresorbable Vascular Scaffold (BVS) System

March 15, 2016

Abbott Vascular

Circulatory System Devices Panel

Absorb GT1™ Bioresorbable Vascular Scaffold (BVS) System

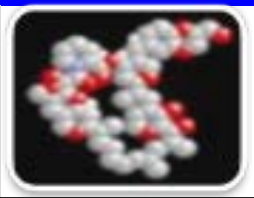
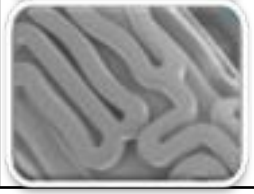
Chuck A. Simonton, MD, FACC, FSCAI

Chief Medical Officer

Divisional Vice President

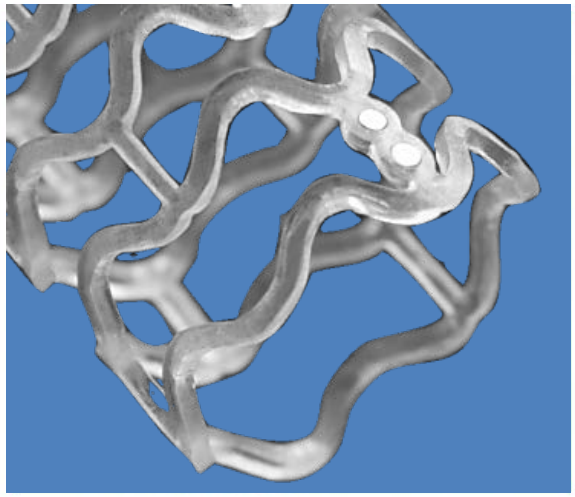
Abbott Vascular

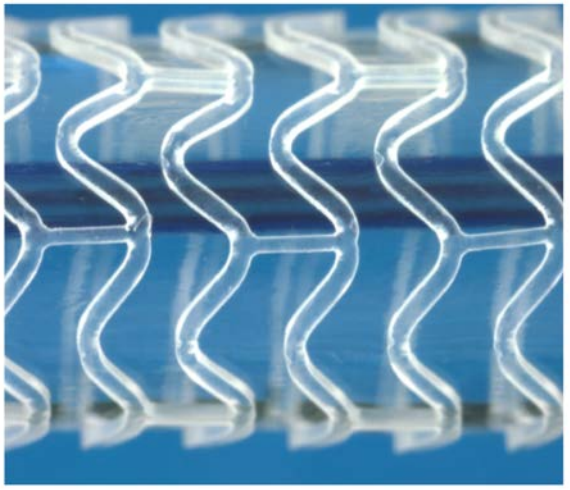
Absorb: 1st Completely Bioresorbable DES, Built upon Xience Technology

Material / Design		Xience	Absorb
Drug / Elution		Everolimus	
Stent / Scaffold Design		MULTI-LINK Design	
Delivery System		MULTI-LINK SDS	
Stent / Scaffold Material		Cobalt Chromium	Poly (L-lactide)
Coating Material		Fluorinated Copolymer	Poly (DL-lactide)

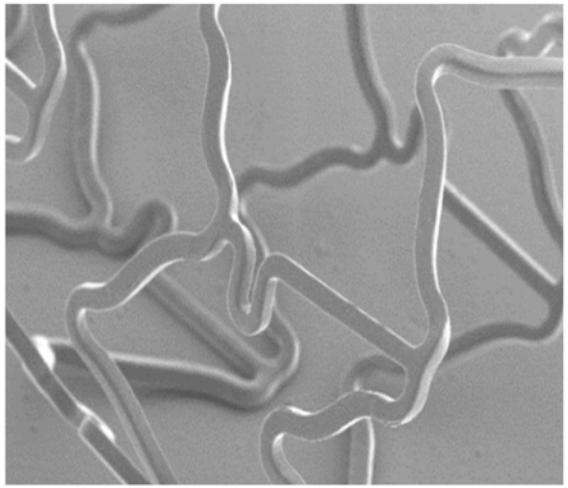
Absorb and Xience Have Similar Implant Designs

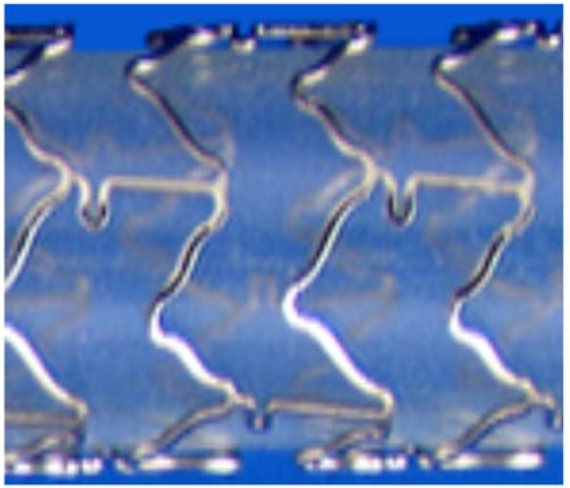
Absorb



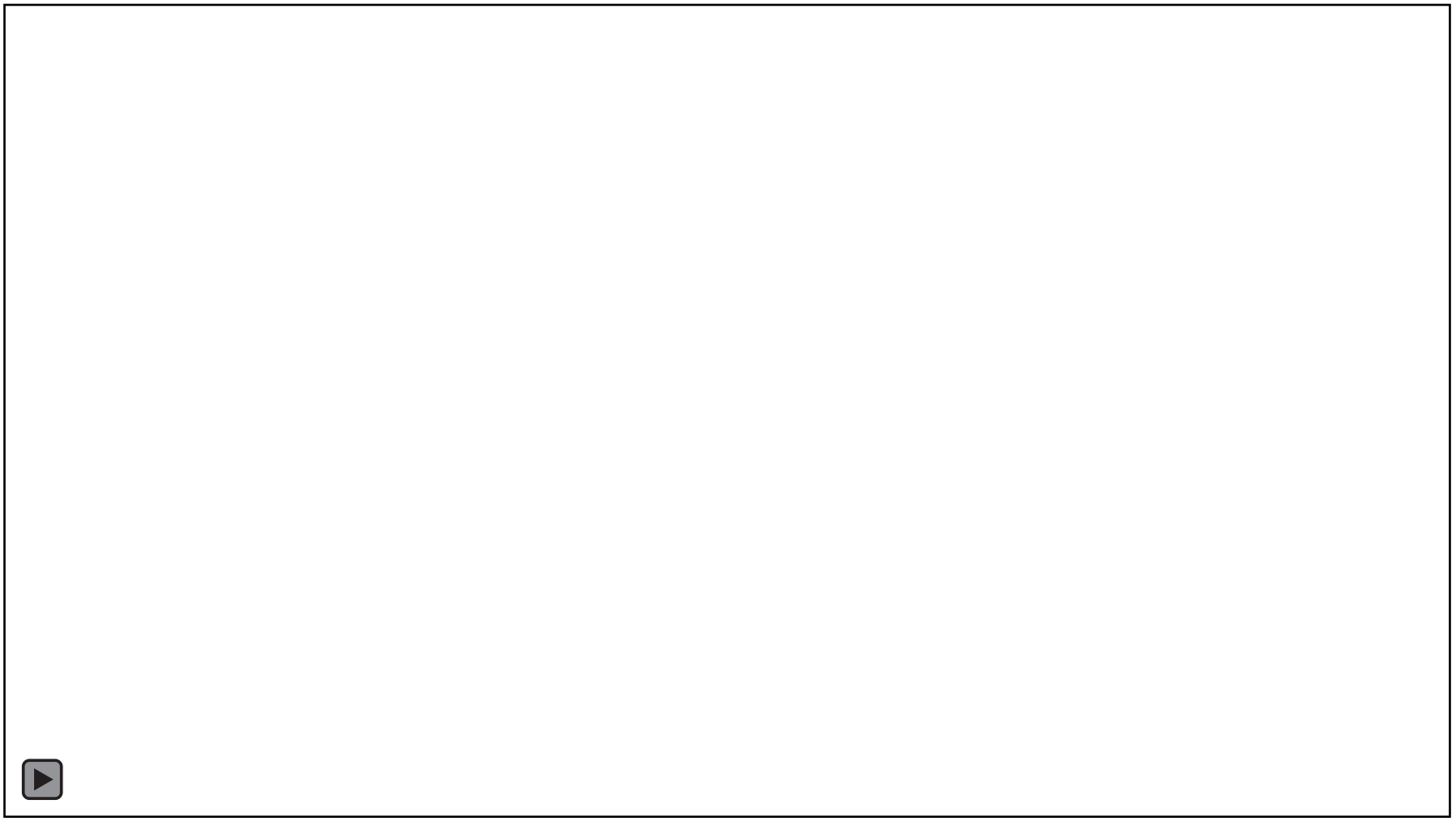


Xience

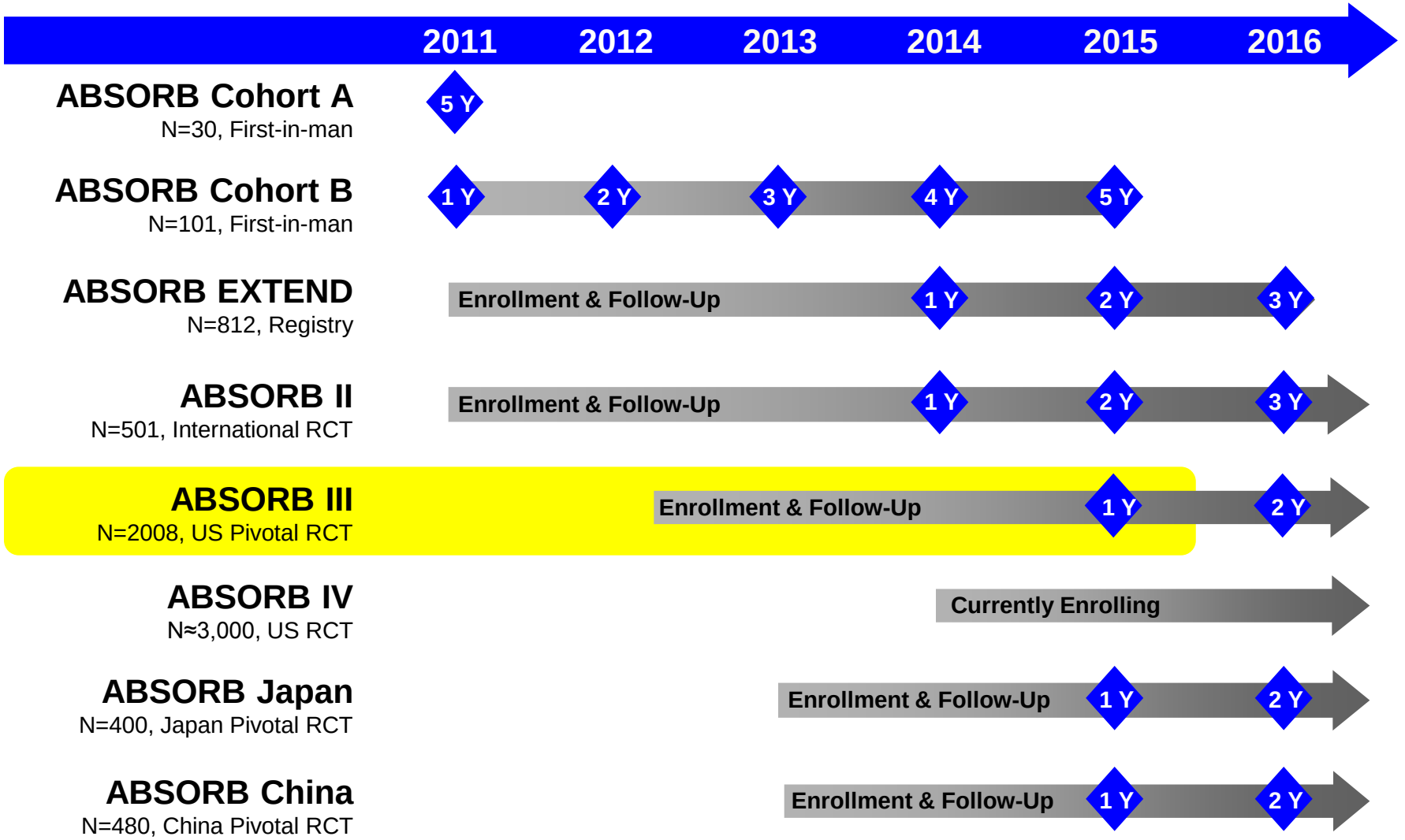




Absorb Uses Same Delivery Technique as Drug-Eluting and Bare Metal Stents



Absorb Clinical Program



Absorb Worldwide Commercial Usage: Over 125,000 Patients Treated

Over 125,000 patients treated to date in over 100 countries

What We Will Demonstrate Today

- ABSORB III met pre-specified primary endpoint demonstrating reasonable assurance of safety and effectiveness
- Met FDA regulatory standards for DES approval
- Absorb is appropriate treatment option for patients who require PCI therapy and do not want permanent implant

Absorb: Proposed Indication for Use

The Absorb GT1 Bioresorbable Vascular Scaffold (BVS) is a temporary scaffold that will fully resorb over time and is indicated for improving coronary luminal diameter in patients with ischemic heart disease due to *de novo* native coronary artery lesions (length ≤ 24 mm) with a reference vessel diameter of ≥ 2.5 mm and ≤ 3.75 mm

Agenda

Technology Overview & Design Rationale	**Chuck Simonton, MD** Abbott Vascular
ABSORB III Trial Design	**Dean J. Kereiakes, MD** The Christ Hospital Heart and Vascular Center
ABSORB III Results: Safety & Effectiveness Absorb Long-term Data High Level Summary: Benefit-Risk Analysis	**Gregg W . Stone, MD** Columbia University
Sponsor Commitments	**Chuck Simonton, MD** Abbott Vascular
Clinical Perspective	**Mitchell W. Krucoff, MD** Duke University

Additional Experts

Non-Abbott Vascular

- **Stephen Ellis, MD**
  Director of Interventional Cardiology
  Senior Academic Officer
  Sydell and Arnold Miller Family Heart & Vascular Institute, Cleveland Clinic

- **Christoph Kurt Naber, MD**
  Assoc. Professor of Medicine
  Director of Department of Cardiology and Angiology, Contilla Heart and Vascular Center
  Essen Germany

- **Stuart Pocock, PhD**
  Professor of Medical Statistics
  London School of Hygiene and Tropical Medicine

- **Jeffrey J. Popma, MD**
  Director, Interventional Cardiology Clinical Services
  Beth Israel Deaconess Medical Center
  Professor of Medicine, Harvard Medical School

Abbott Vascular

- **Laura Perkins, PhD, DVM, DACVP**
  Research Scientist
  Preclinical Research and Biocompatibility

- **Richard Rapoza, PhD**
  Divisional Vice President
  Research & Development

- **Zhen Zhang, PhD**
  Associate Director
  Worldwide Biometrics

Technology Overview & Design Rationale

Chuck Simonton, MD, FACC, FSCAI

Chief Medical Officer

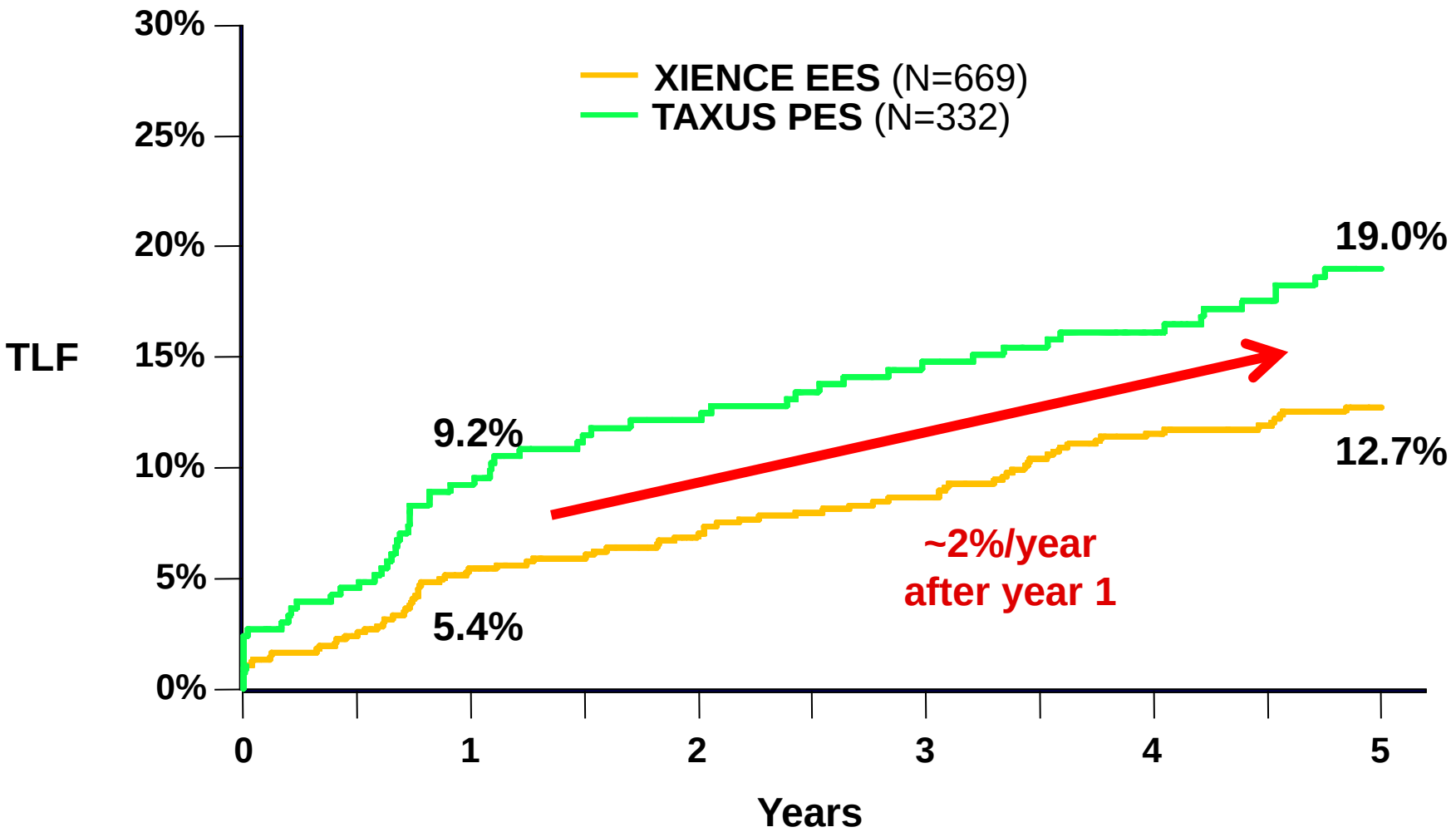
Divisional Vice President

Abbott Vascular

Evolution of Percutaneous Coronary Intervention (PCI) Treatments

Plain Old Balloon Angioplasty (POBA) ’85-’95	Bare Metal Stent ’95-’03	Metallic Drug Eluting Stent ’03-’16
		
Advantages		
• Low profile • Easy to use	• Reduces acute closure and restenosis	• Further reduces late restenosis
Disadvantages		
• Dissection • Acute closure • Restenosis	• Permanent implant • Thrombosis and restenosis	• Permanent implant • On-going risk of very late restenosis and thrombosis

SPIRIT III: TLF to 5 Years



Gada H et al. (2013); TLF = cardiac death, target vessel MI, or ischemic-driven TLR

Limitations of Permanent Metallic Drug-Eluting Stents

- Permanently covers side branches, limiting access
- Prevents insertion of bypass grafts
- Multiple stent layers reduce vessel diameter
- Commits patient to life-long implant for treatment of temporary problem
  - Many patients and physicians wish to avoid permanent implant

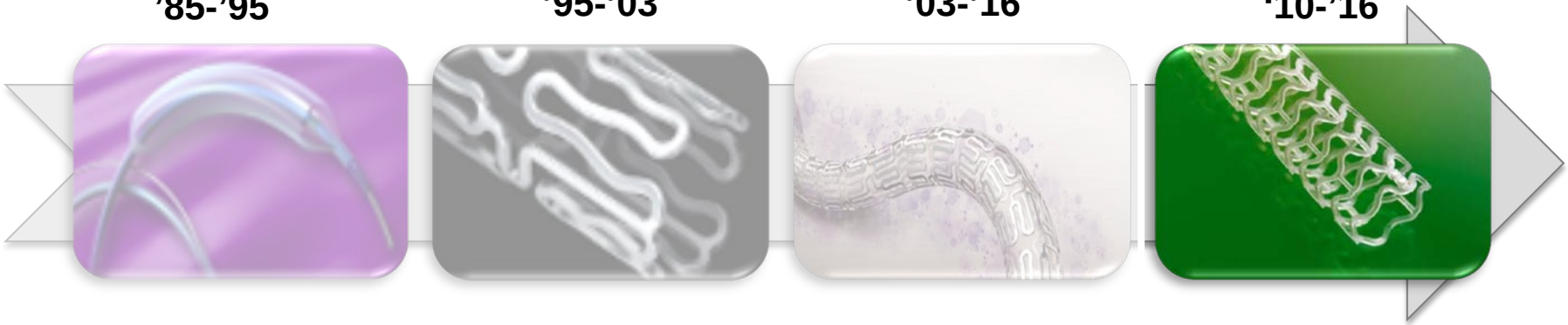
Evolution of Percutaneous Coronary Intervention (PCI) Treatments

Plain Old Balloon Angioplasty (POBA)
’85-’95

Bare Metal Stent
’95-’03

Metallic Drug Eluting Stent
’03-’16

Bioresorbable Scaffold
‘10-’16



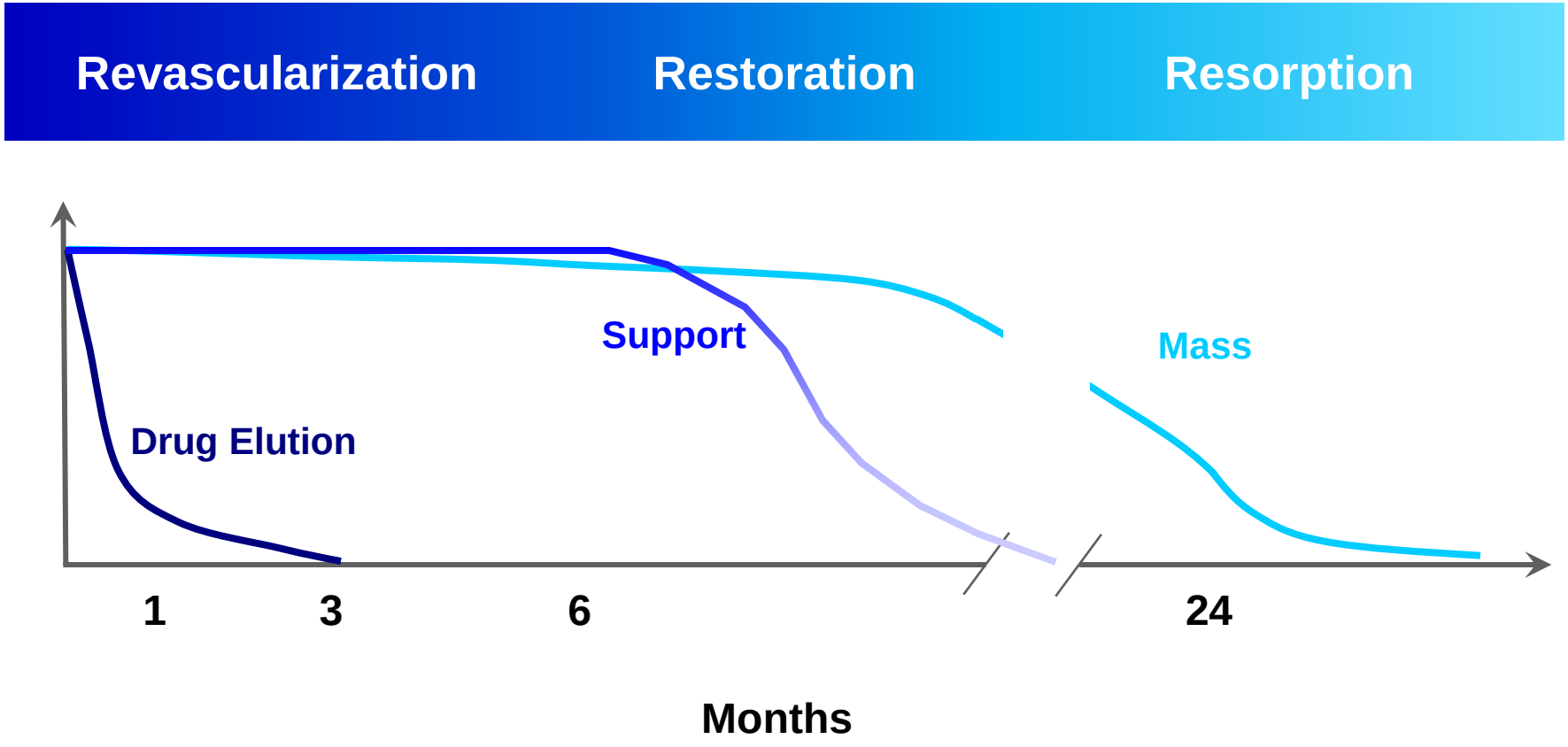
Advantages

- Reduction in long-term events due to no permanent implant

Absorb Design Objectives

- Achieve similar results as metallic DES within 1st year
- Allow for more normal vessel recovery and healing (over time with resorption)
- Provide physicians with option to treat patients without a permanent implant

Phases of Absorb Functionality



Absorb Performance: Characteristics Similar to Xience

REVASCULARIZATION
Acute recoil
Radial strength
Everolimus elution and pharmacokinetics
Low and acceptable thrombogenicity
Healing (endothelialization)

Absorb Performance: Characteristics Unique to Absorb

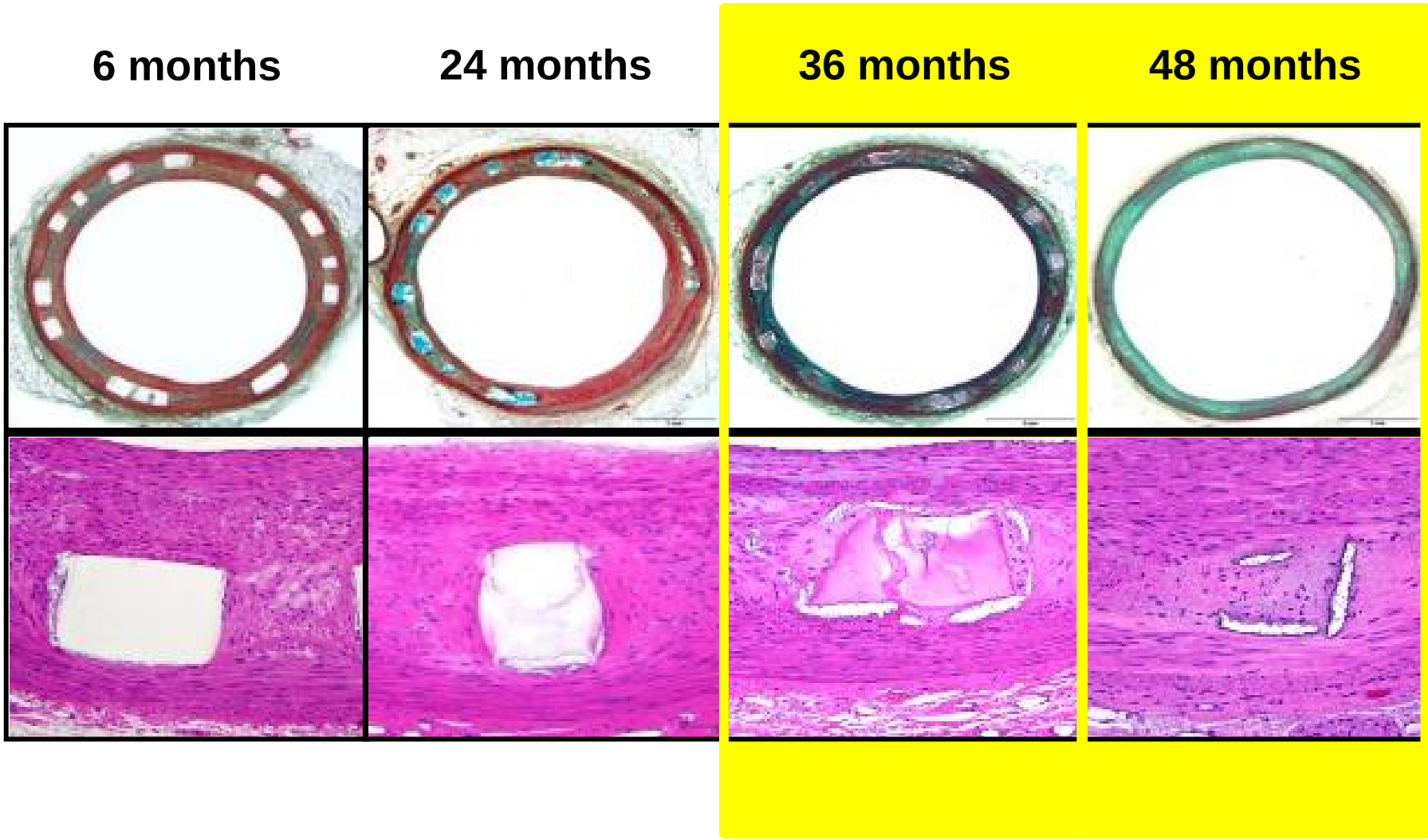
RESTORATION
Gradual loss of radial strength after 6 months
Return of pulsatility and vasomotion
Lumen enlargement over time[1]
RESORPTION
Complete scaffold resorption[1]

1. Otsuka, F., et al. (2014). Circ Cardiovasc Interv 7: 330-342

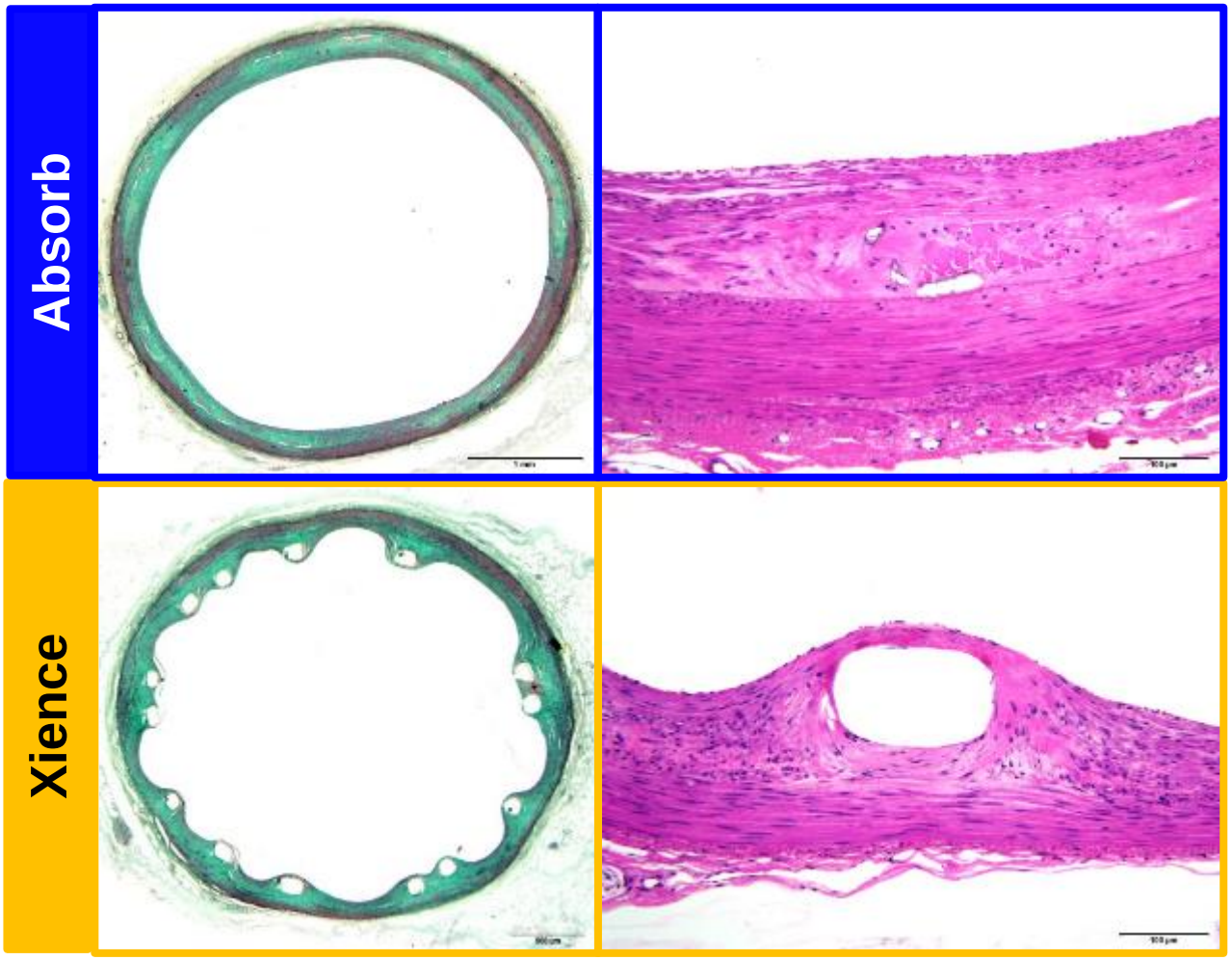
Preclinical Evidence

1. Complete Resorption
2. Recovery of Vessel Function
3. Lumen Enlargement

Full Bioresorption of Scaffold: Porcine Histology

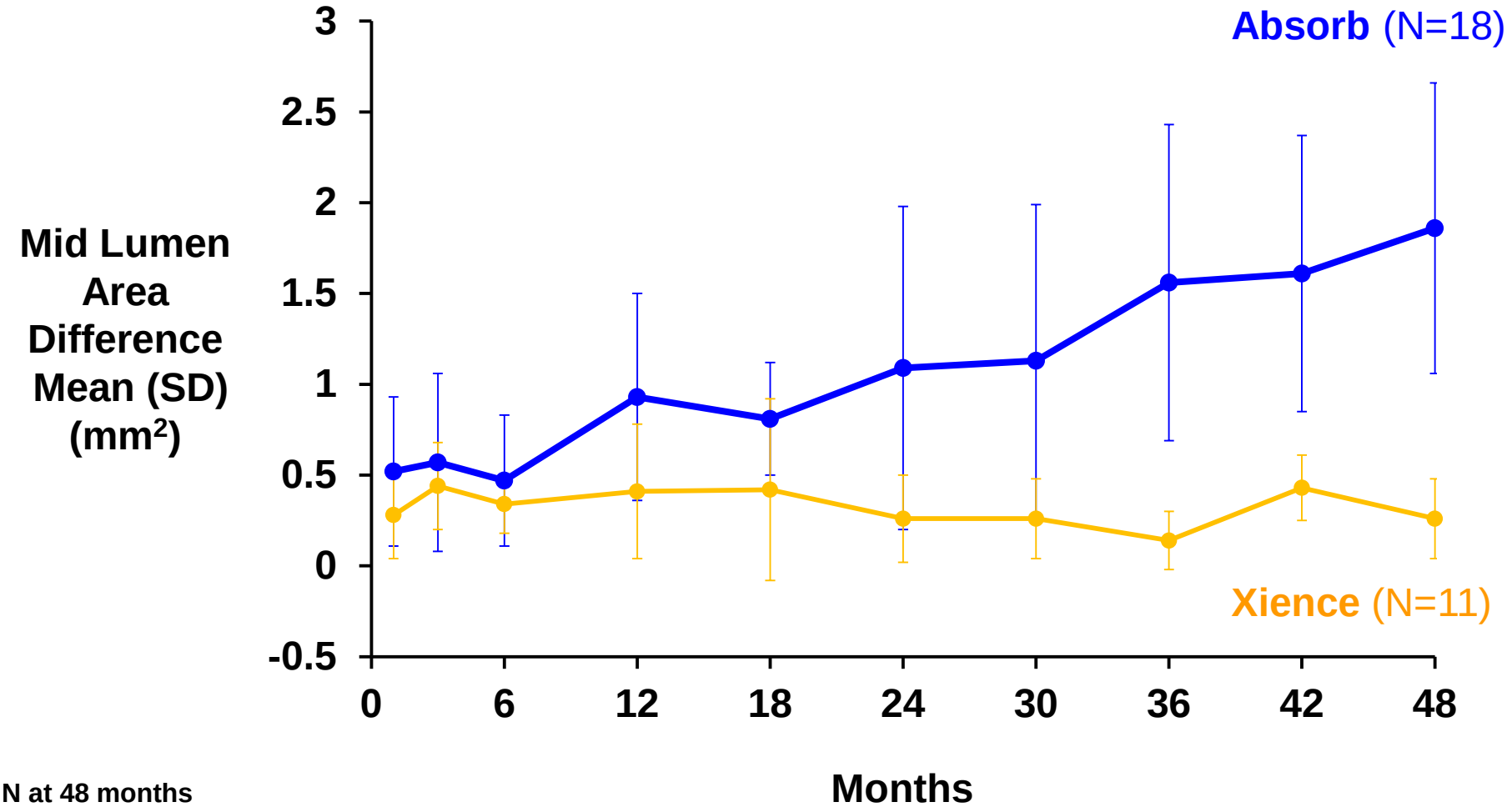


Absorb Struts Replaced by Tissue: Porcine Histology through 48 Months



Representative photomicrographs of porcine coronary arteries 48 months post-implant, 2x Movat's pentachrome and 20x HE

Increase of Pulsatility Over Time: Porcine Data

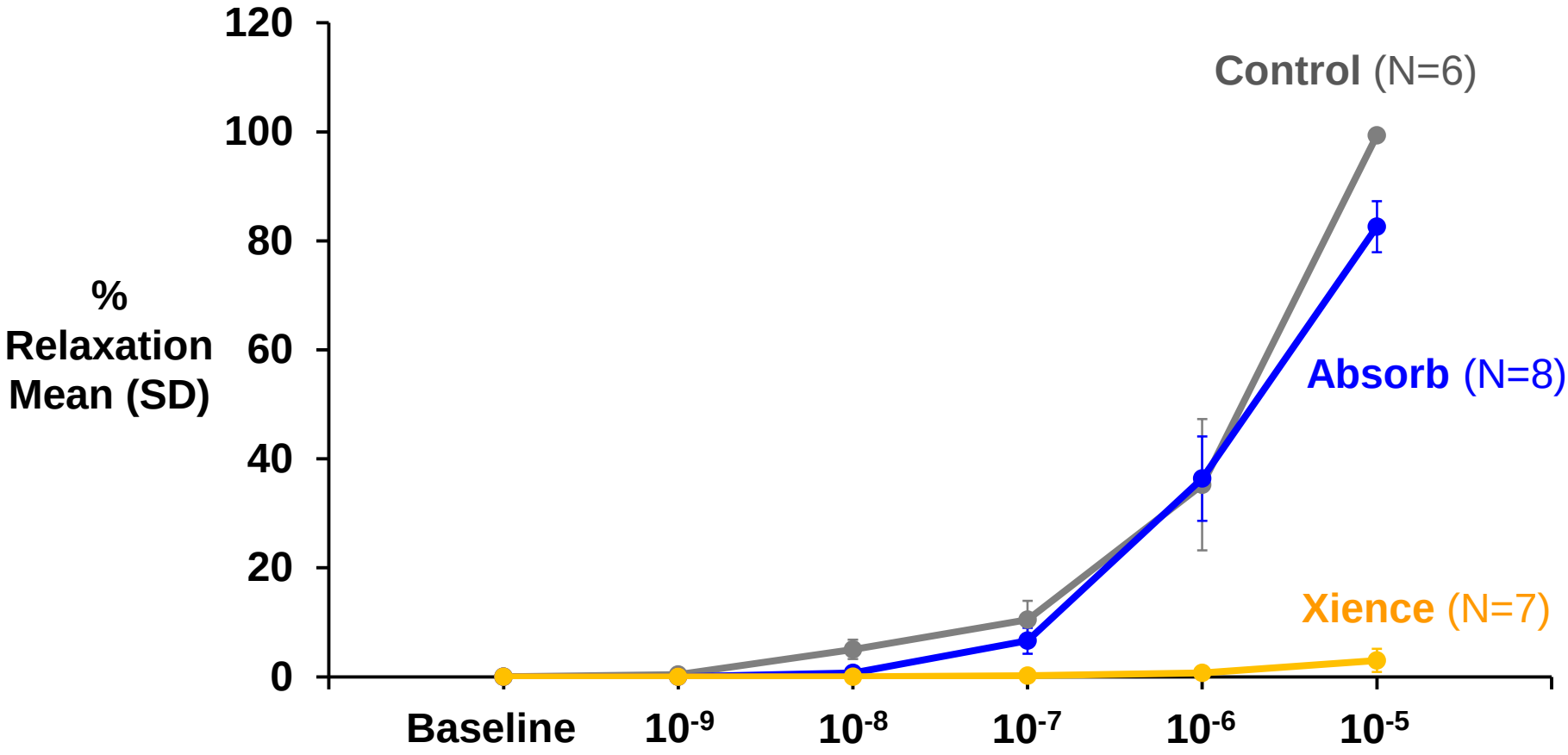


N at 48 months

Lane et al. J Am Coll Cardiol Intv. 2014;7(6):688-695

Pulsatility defined as difference in change in mean lumen diameter of implanted region between end-diastole and -systole

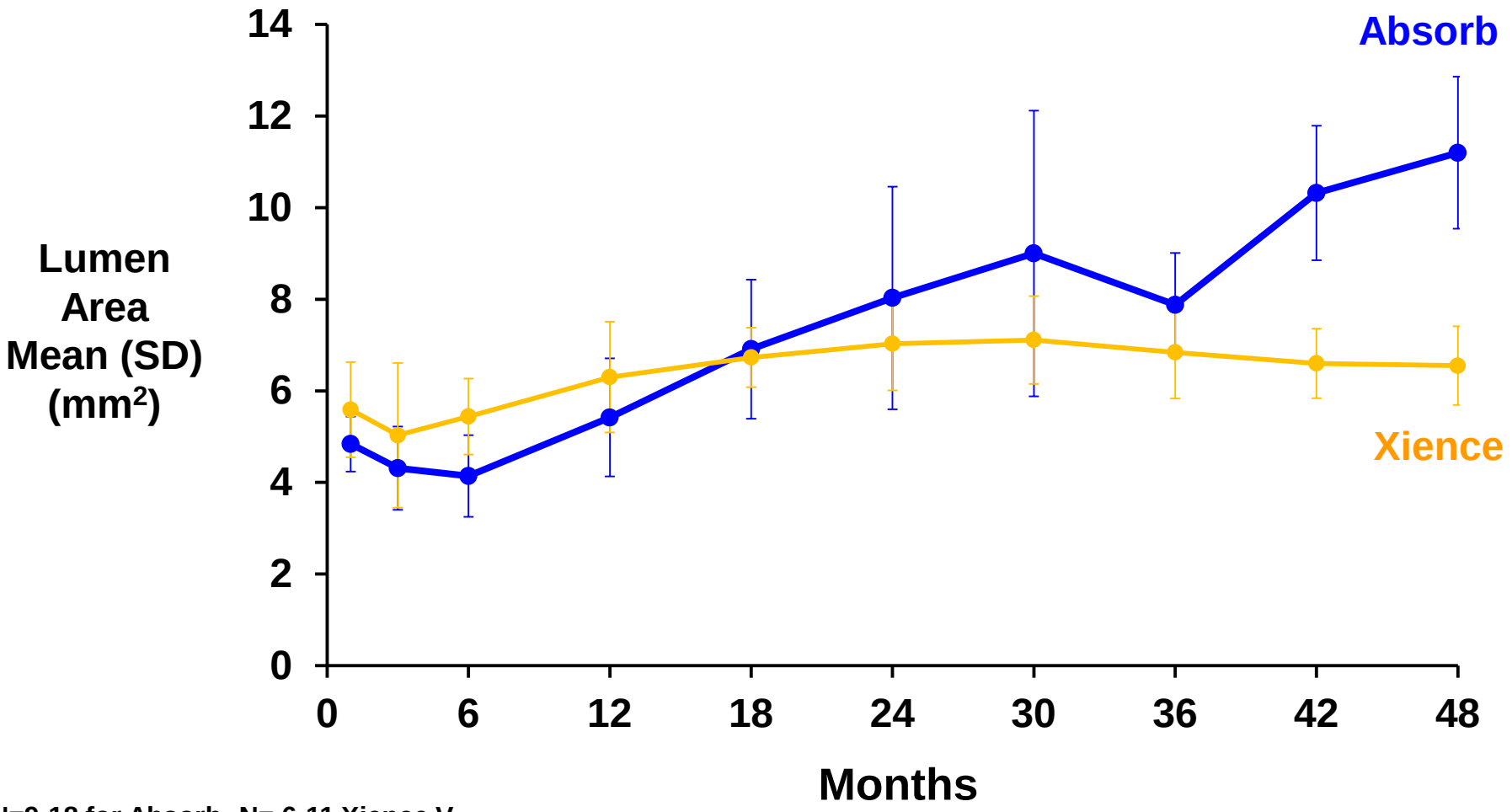
Restored Vasomotion with Absorb at 2 Years: Porcine Data



Based on ex vivo porcine arterial tissue
Adapted from Gogas et al. JACC 2015

Data/analysis not submitted or reviewed by FDA

Late Lumen Enlargement of Absorb Arteries: Porcine IVUS Data



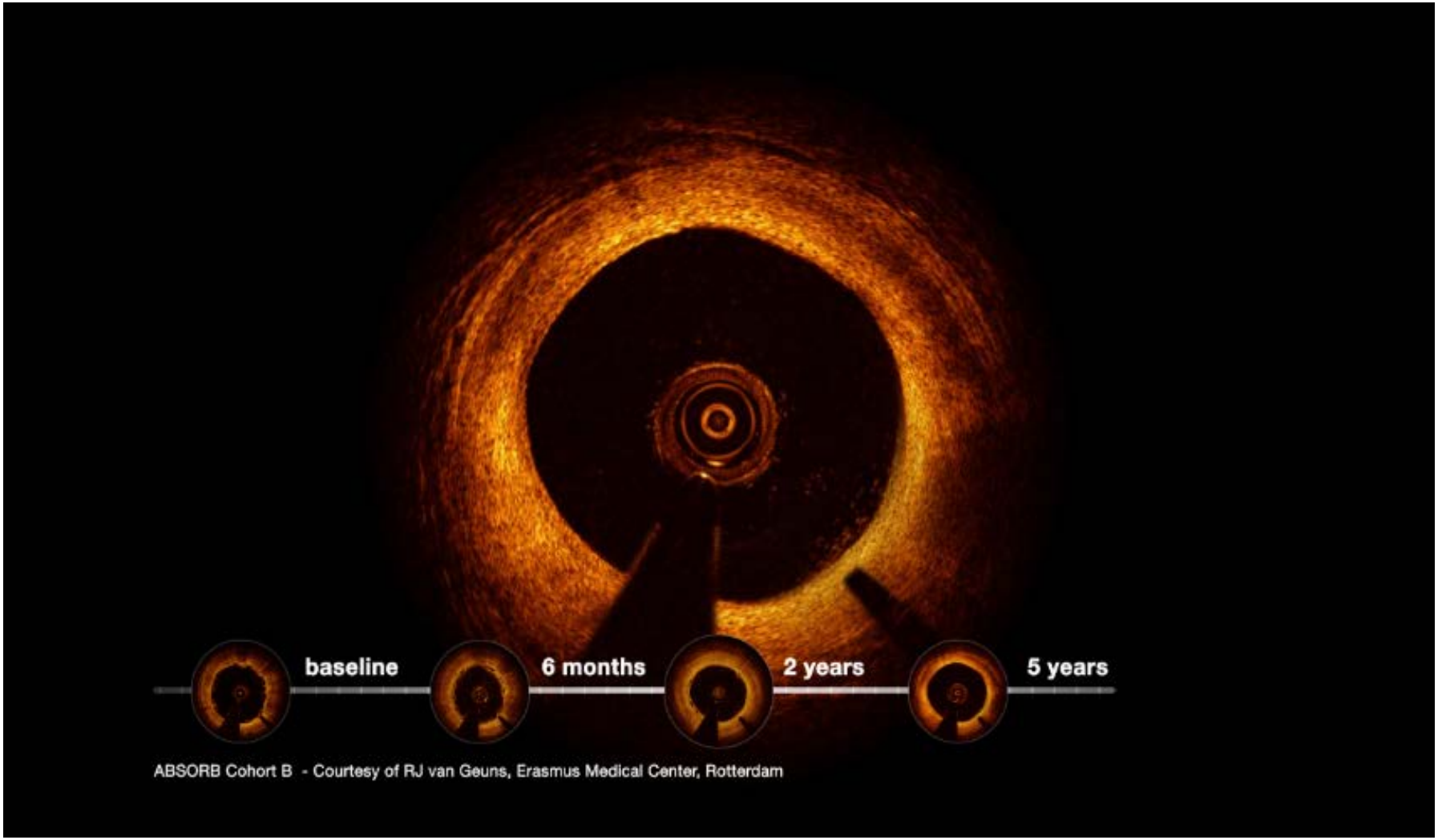
N=9-18 for Absorb; N= 6-11 Xience V

Lane et al. J Am Coll Cardiol Intv. 2014;7(6):688-695

Early Human Studies: ABSORB Cohort B

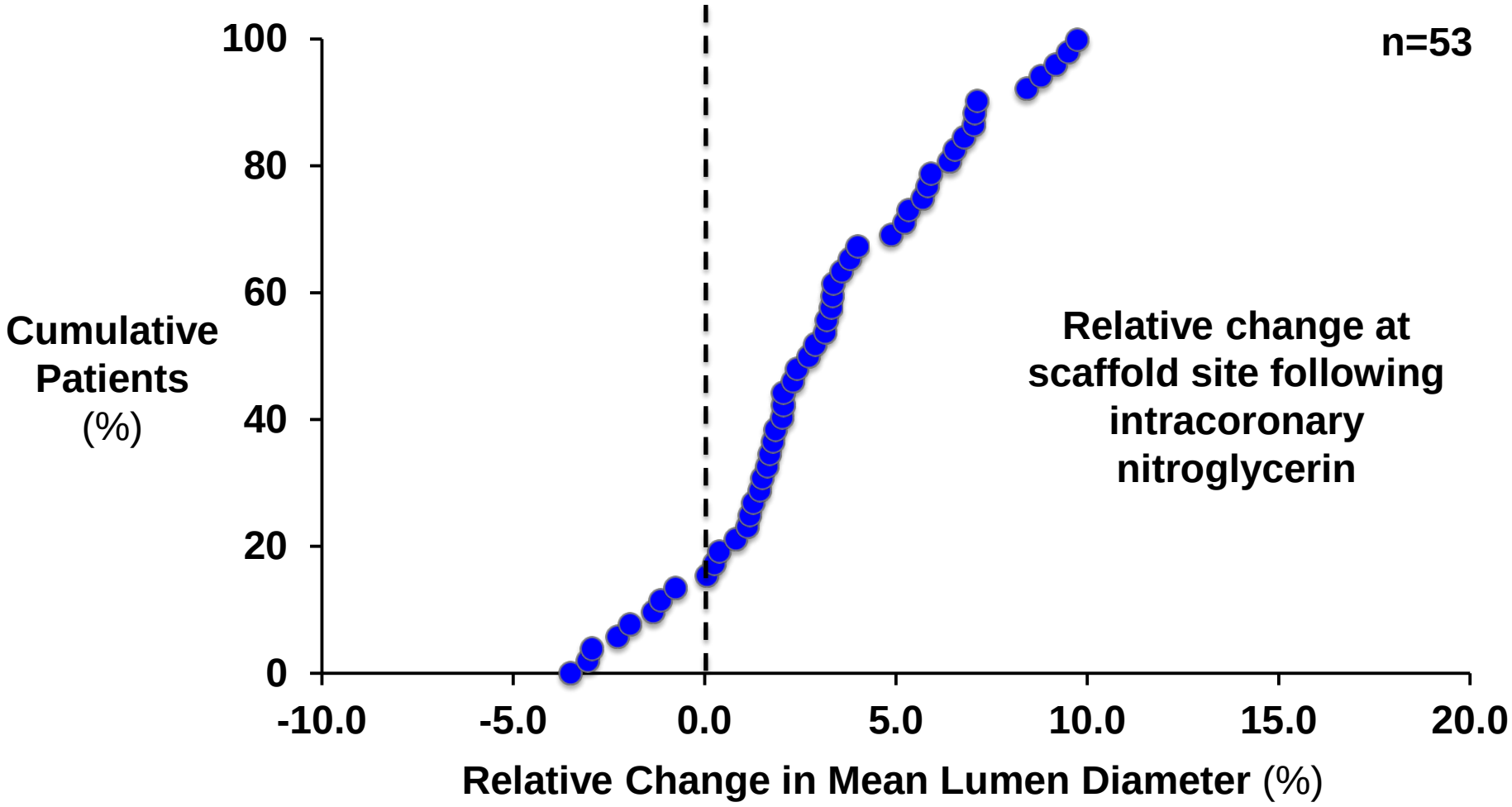
1. Complete Resorption
2. Recovery of Vessel Function
3. Lumen Enlargement

Full Scaffold Resorption and Lumen Preservation at Long-Term Follow-Up



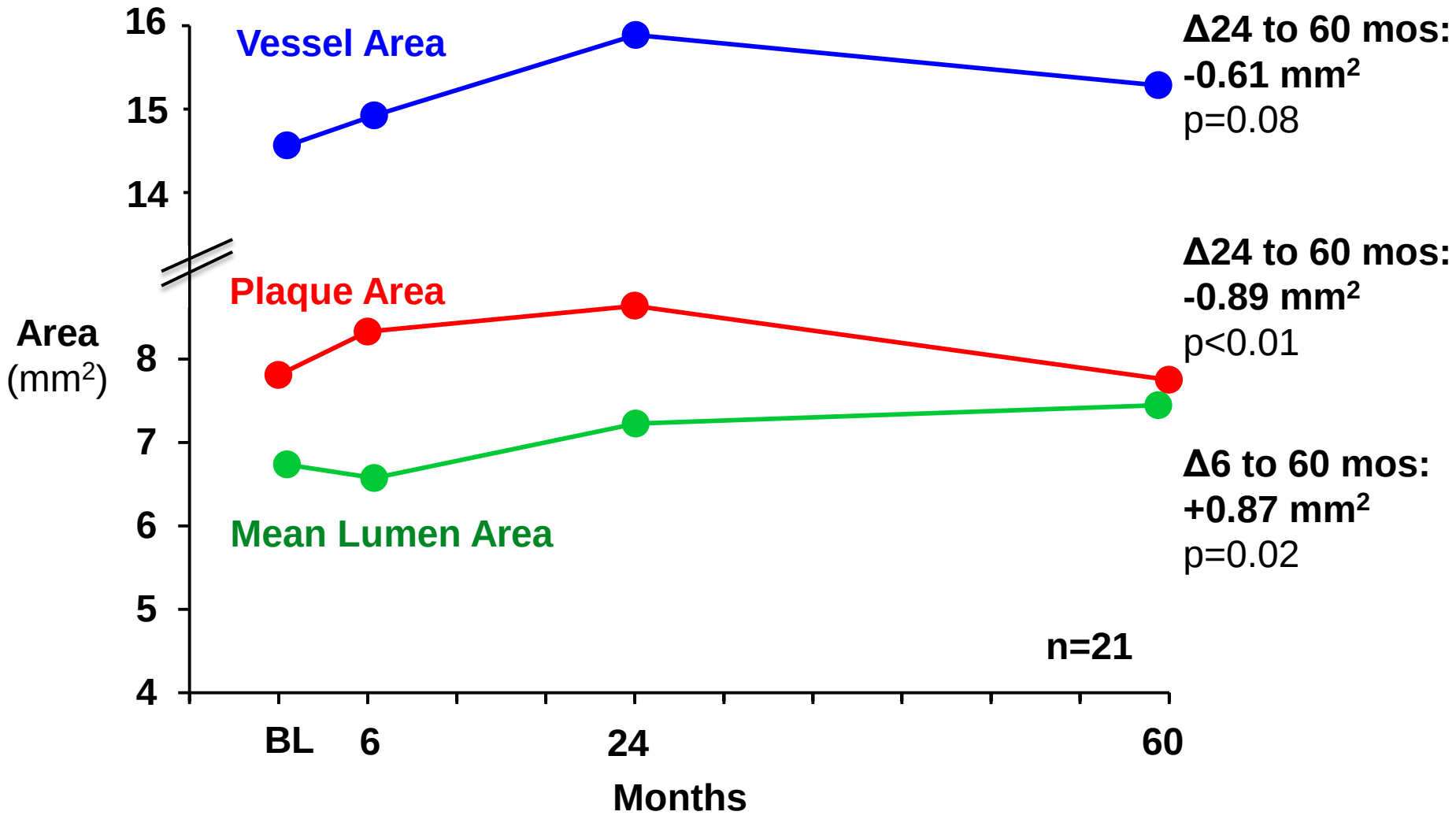
Data/analysis not submitted or reviewed by FDA

Restored Vasomotion at 5 Years in ABSORB Cohort B



Adapted from Serruys and Onuma TCT 2015
Relative change = 100 x (mean LD post Nit-mean LD pre Nit) / mean LD pre Nit

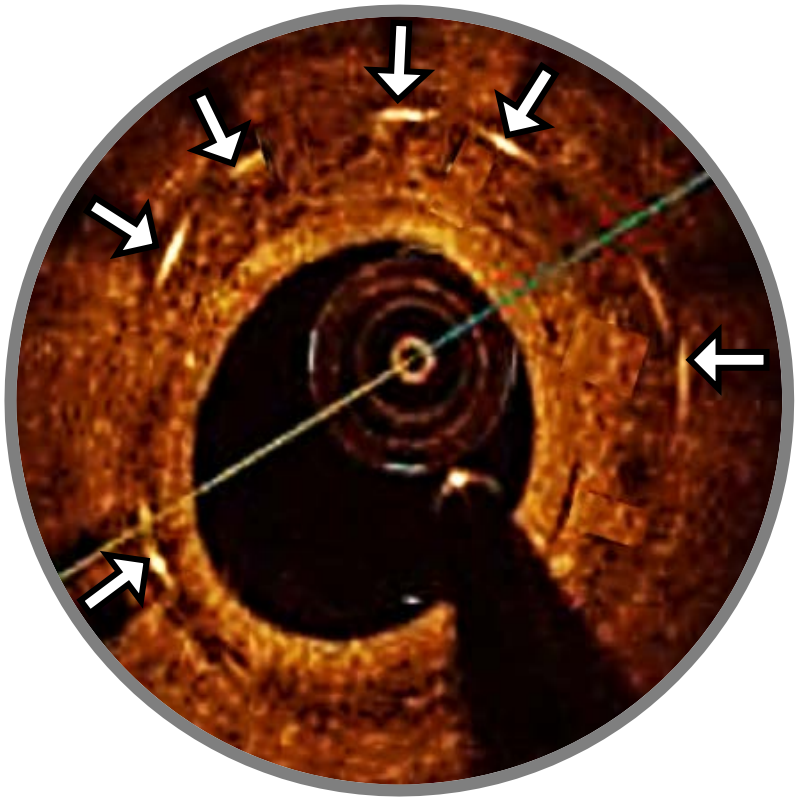
Lumen Preservation Over 5 Years in ABSORB Cohort B



Serruys and Onuma TCT 2015

Metallic DES vs. Absorb: Representative Human Images at 5 Years

Metallic DES[1]



Absorb[2]

1. Atherosclerosis 2014;237:23e29
2. Image courtesy of S Windecker, ABSORB Cohort B 5 years

Summary

- Absorb represents logical step in PCI evolution
- Absorb provides similar mechanical support as Xience with additional novel properties
- Preclinical evidence demonstrates
  - Complete resorption
  - Recovery of vessel function
  - Lumen enlargement
- Previous clinical studies support preclinical findings in human patients

ABSORB III Trial Design

Dean J Kereiakes, MD, FACC, FSCAI

The Christ Hospital Heart and Vascular Center

Cincinnati, OH

Trial Objective

- To demonstrate Absorb is comparable (i.e. non-inferior within an acceptable margin) to DES (Xience) at 1 year

ABSORB III Trial Designed Using FDA Guidance

1. Non-inferiority (NI) design to demonstrate Absorb is non-inferior to FDA-approved DES
2. Use of Target Lesion Failure (TLF) as primary outcome measure to evaluate a combination of safety and effectiveness at 1 year
3. NI margin for statistical analysis based on current FDA guidance on NI clinical trials

Trial Design

- Prospective, single-blind, multi-center RCT
- 193 sites
- Randomized 2:1
  - Absorb N=1322
  - Xience N=686
- Xience chosen as comparator because it is among the best-in-class for clinical outcomes

Available Device Sizes in ABSORB III

	Diameters (mm)	Lengths (mm)
Absorb[1]	2.5, 3.0, 3.5	8, 12, 18, 28
Xience[2]	2.5, 2.75, 3.0, 3.25, 3.5, 4.0	8, 12, 15, 18, 23, 28

1. Both 8 and 12 mm lengths were available for 2.5 and 3.0 mm diameter; 8 mm length not available for 3.5 mm diameter
2. Xience family of stents: XIENCE V, XIENCE PRIME, and XIENCE Xpedition

Composite Primary Endpoint: Safety and Effectiveness

TLF at 1 Year (Intention-to-Treat):

1. **Cardiac death**
   - Any death suspected to be cardiac in nature
2. **MI attributable to target vessel (TV-MI)**
   - Peri-procedural: CK-MB > 5x ULN w/in 48 hours from index procedure
   - Spontaneous: Troponin or CK-MB > ULN plus evidence of ischemia

Safety

3. **Ischemia-driven target lesion revascularization (ID-TLR)**
   - Any repeat PCI of target lesion or CABG of target vessel with evidence of ischemia

Effectiveness

Analysis Populations

- **Intention-to-Treat (ITT) Primary Analysis Population**
  - All patients in study at randomization. Analyzed in group they were randomized to, regardless of treatment actually received
- **Per-Treatment Evaluable (PTE)**
  - Patients who received only study device(s) (Absorb or Xience) at target lesion, excluding those with specific protocol deviations
- **As-Treated (AT)**
  - Analyses based on treatment (Absorb or Xience) actually received

Key Patient Eligibility

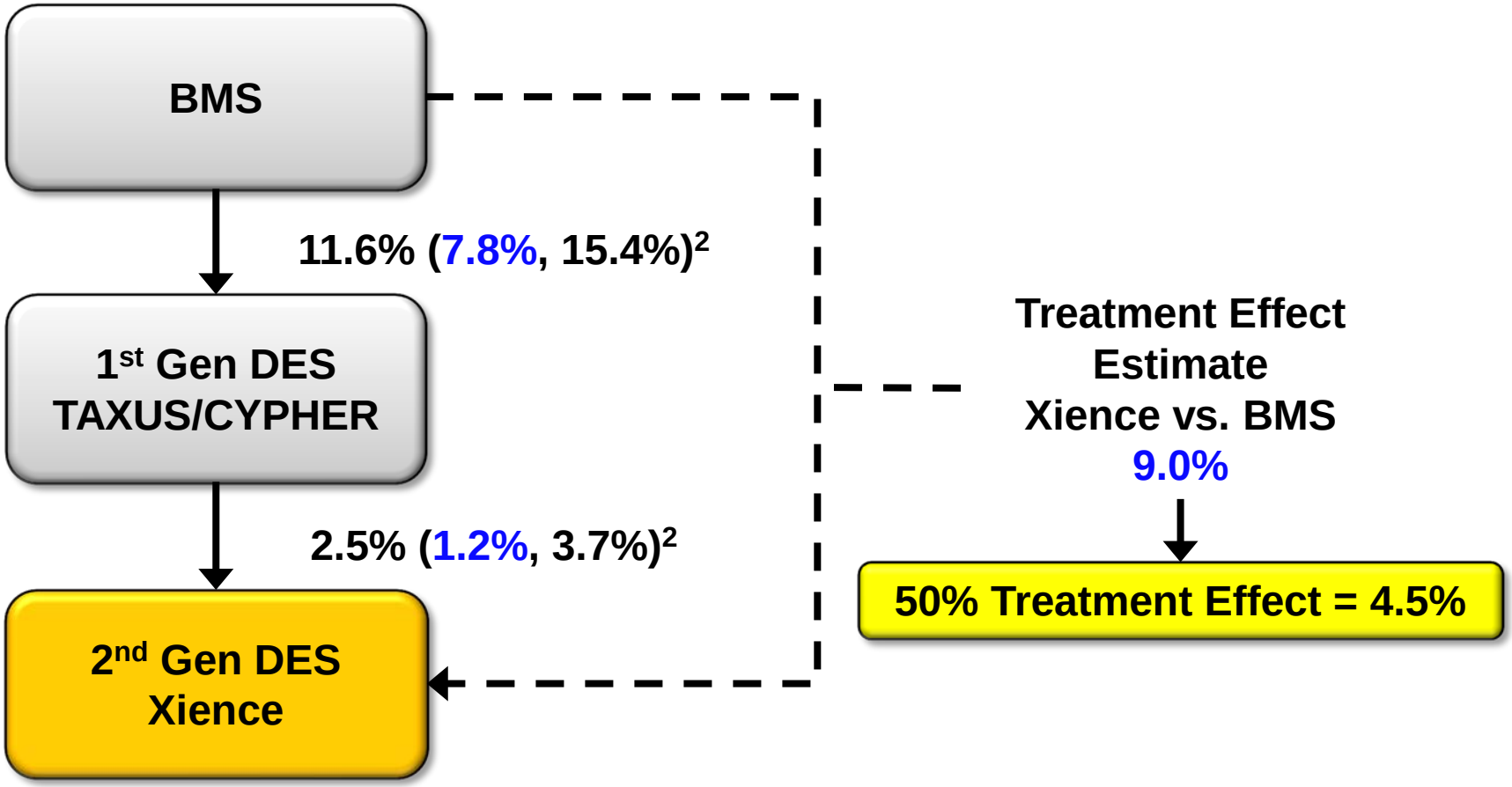
- ≥ 18 years old
- Evidence of myocardial ischemia (stable, unstable and post-infarct angina or silent ischemia)
- No elevation in CK-MB
- 1 or 2 *de novo* target lesions in up to 2 native coronary arteries (max 1 lesion per artery)
- Diameter stenosis (DS)
  - ≥ 50% and < 100% with a TIMI flow of ≥ 1
  - If < 70%, patient must have abnormal functional test, (including FFR ≤ 0.80), unstable or post-infarct angina
- Reference vessel diameter (visual estimation at site)
  - ≥ 2.50 mm and ≤ 3.75 mm and lesion length ≤ 24 mm

Statistical Design

Non-inferiority analysis for TLF at 1 year (ITT population) with following assumptions:

- 1-Year TLF rate of 7%
  - Based on similar patients from SPIRIT IV (N=2051)
  - TV-MI adjusted according to ABSORB III MI definition
- Non-inferiority margin of 4.5%
  - "Putative placebo", preserving ≥ 50% of treatment effect of Xience vs. BMS
- One-sided alpha of 0.025
- 2000 subjects → 96% power

Derivation of NI Margin Based on Meta-analysis[1] of Historical Trials



1. Random effect meta-analysis (Dersimonian and Laird method)
2. Two-sided 90% confidence interval

Powered Secondary Endpoints

- Test hypothesis that Absorb may reduce:
  1. Angina at 1 year
     - First AE resulting in diagnosis of angina
     - Excludes angina following index procedure, not to exceed 7 days
  2. All revascularization at 1 year
  3. Ischemia-driven target vessel revascularization (ID-TVR) at 1 year

Sequential testing of powered secondary endpoints

Other Secondary Endpoints

- Major adverse cardiac events (MACE)
  - Cardiac death, MI, ID-TLR
- Target vessel failure (TVF)
  - Cardiac death, MI, ID-TLR, ID-TVR (non-target lesion)
- Death, MI, all revascularization
- Cardiac death/MI
- Stent or scaffold thrombosis (ST)
  - ARC definite/probable

Trial Management

- **Angiographic Core Laboratory**
  - Director: **Dr. Jeff Popma**
    Beth Israel Deaconess Medical Center
    Angiographic Core Laboratories, Boston, MA
- **Clinical Events Committee**
  - Director: **Dr. Steven Marx**
    Cardiovascular Research Foundation
    New York, NY
- **Data Safety Monitoring Board**
  - Chairman: **Dr. Robert N. Piana**
    Vanderbilt University Medical Center
    Nashville, TN

ABSORB III Results: Safety & Effectiveness

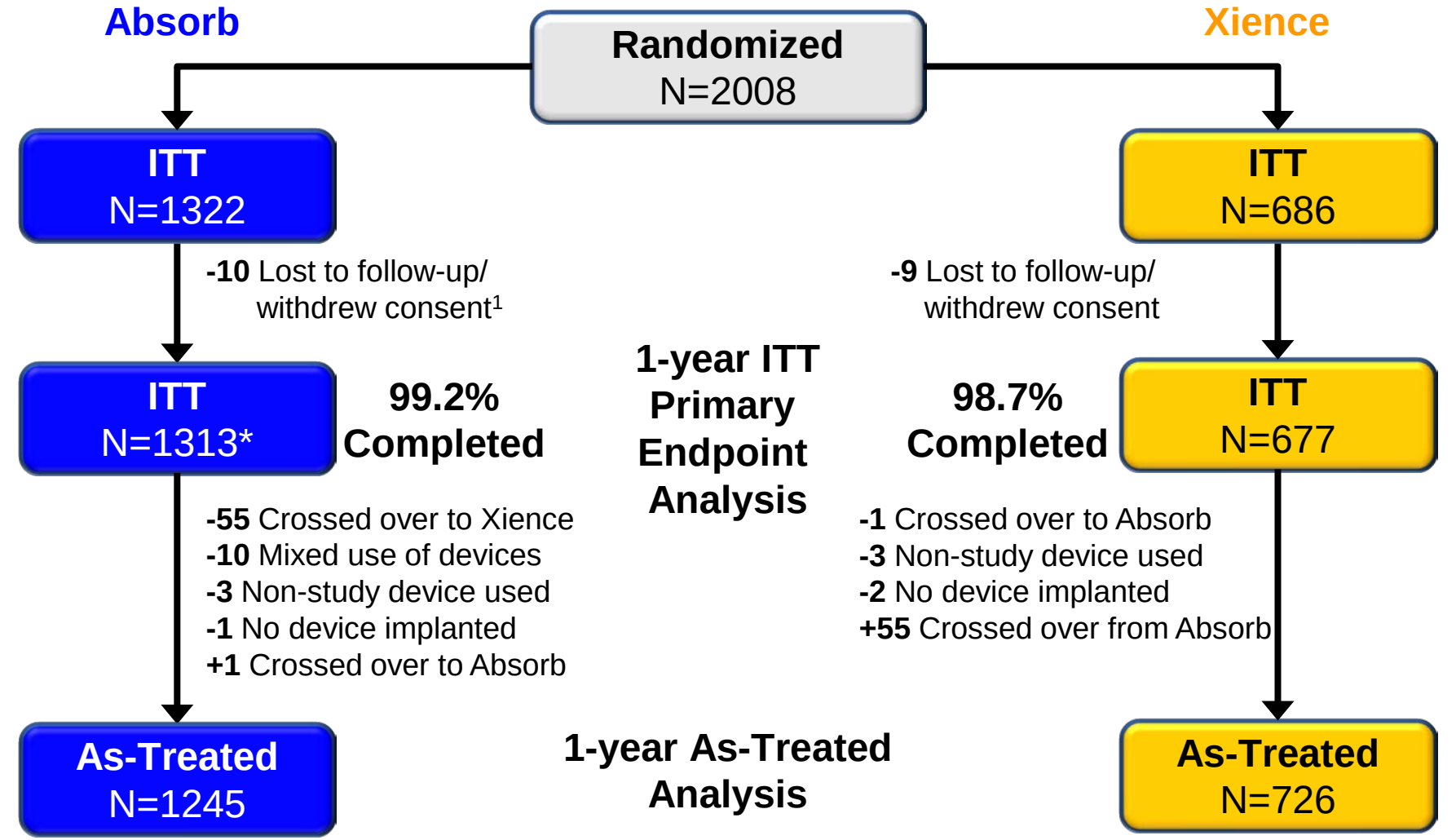
Gregg W Stone, MD

Columbia University Medical Center

The Cardiovascular Research Foundation

New York, NY

Clinical Follow-up ~99% for Both Absorb and Xience Arms



1. One of the six withdrawals had an event and therefore was included in the 1-year follow-up

Baseline Characteristics: Similar Between Absorb and Xience Groups

Characteristic	Absorb N=1322	Xience N=686
Age (mean)	63.5 ± 10.6	63.6 ± 10.3
Male	70.7%	70.1%
Diabetes	31.5%	32.7%
Current tobacco use	21.3%	20.7%
Hypertension	84.9%	85.0%
Dyslipidemia	86.2%	86.3%
Prior MI	21.5%	22.0%
Clinical presentation		
Stable CAD	70.3%	72.9%
Recent ACS or MI	29.7%	27.1%

Ellis SG et al. N Engl J Med. 2015;373:1905-15

Similar Vessel & Lesion Characteristics Between Groups

Characteristic	Absorb N=1322 L=1385	Xience N=686 L=713
Target Vessel		
Left anterior descending	44.5%	42.2%
Right coronary artery	29.2%	27.2%
Left circumflex or ramus	26.2%	30.6%
ACC/AHA Lesion Class B2/C	68.7%	72.5%
Pre-Procedure QCA		
Lesion length, mm	12.6 ± 5.4	13.1 ± 5.8
Reference vessel diameter, mm	2.67 ± 0.45	2.65 ± 0.46
Minimal lumen diameter, mm	0.92 ± 0.37	0.90 ± 0.34
%DS	65.3 ± 12.5	65.9 ± 11.7

N = Patients; L = Lesions; Ellis SG et al. N Engl J Med. 2015;373:1905-15

Peri-procedural Antiplatelet Agent and Anticoagulation Use

	Absorb N=1322	Xience N=686	
	%	%	p-value
Aspirin	99.3	99.3	1.00
P2Y12 inhibitor loading	99.0	98.8	0.70
Clopidogrel	62.6	64.7	0.34
Prasugrel or ticagrelor	36.5	34.4	0.34
Bivalirudin	60.7	58.7	0.39
Glycoprotein IIb/IIIa inhibitor	10.1	12.4	0.11

Ellis SG et al. N Engl J Med. 2015;373:1905-15

Procedure (I)

Characteristic	Absorb N=1322 L=1385	Xience N=686 L=713	p-value
Total device length, mm	20.5 ± 7.2	20.7 ± 9.0	0.56
Post-dilatation	64.8%	49.9%	<0.0001
Max device diameter, mm	3.18 ± 0.43	3.12 ± 0.45	0.007
Max balloon pressure, atm	15.4 ± 3.0	15.4 ± 3.2	0.83
Intravascular imaging guidance	11.2%	10.8%	0.81

N = Patients; L = Lesions; Ellis SG et al. N Engl J Med. 2015;373:1905-15

Procedure (II)

Characteristic	Absorb N=1322 L=1385	Xience N=686 L=713	p-value
Final Results (QCA)			
Reference vessel diameter, mm	**2.70 ± 0.45**	**2.68 ± 0.47**	**0.33**
In-device			
Acute gain, mm	**1.45 ± 0.45**	**1.59 ± 0.44**	**<0.0001**
Minimal lumen diameter, mm	**2.37 ± 0.40**	**2.49 ± 0.40**	**<0.0001**
% Diameter stenosis	**11.6 ± 8.8**	**6.4 ± 8.9**	**<0.0001**
In-segment			
Acute gain, mm	**1.23 ± 0.46**	**1.24 ± 0.44**	**0.50**
Minimal lumen diameter, mm	**2.15 ± 0.41**	**2.14 ± 0.43**	**0.58**
% Diameter stenosis	**20.0 ± 7.9**	**19.8 ± 8.2**	**0.55**

N = Patients; L = Lesions; Ellis SG et al. N Engl J Med. 2015;373:1905-15

Acute Success

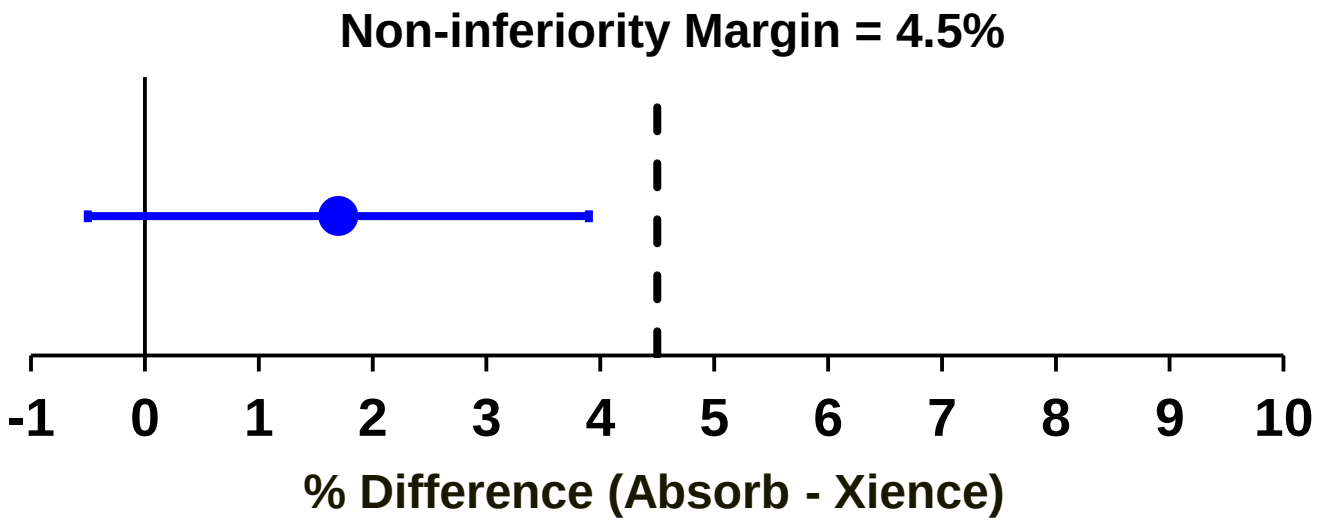
	Absorb N=1322 L=1385	Xience N=686 L=713	p-value
Device Success (per lesion)	**94.3%**	**99.3%**	**<0.0001**
Procedural Success (per patient)	**94.6%**	**96.2%**	**0.12**

- **Device Success (lesion basis)**
  - Successful delivery and deployment of study scaffold/stent at intended target lesion
  - Successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA)
- **Procedure Success (patient basis)**
  - Successful delivery and deployment of at least one study scaffold/stent at intended target lesion
  - Successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA)
  - No in-hospital (maximum 7 days) TLF

N = Patients; L = Lesions; Ellis SG et al. N Engl J Med. 2015;373:1905-15

ABSORB III Met Primary Endpoint: Non-Inferior to Xience in 1-Year TLF (ITT)

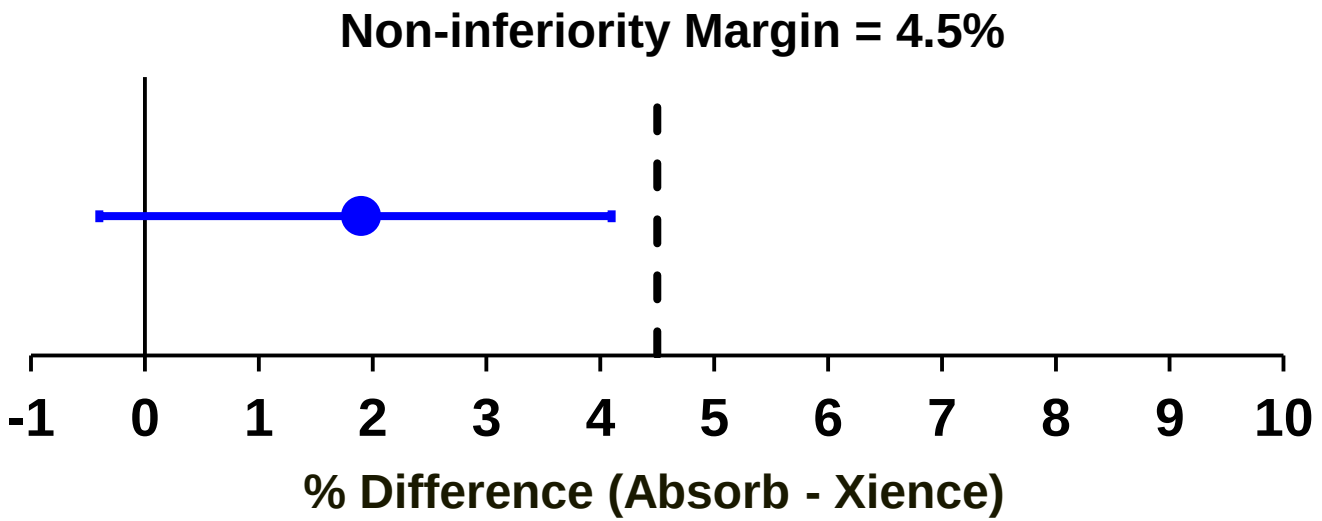
ITT Population	n / N	%	Difference (95% CI)	P_{NI}
Absorb	102 / 1313	7.8	1.7 (-0.5 , 3.9)	0.007
Xience	41 / 677	6.1		



Ellis SG et al. N Engl J Med. 2015;373:1905-15

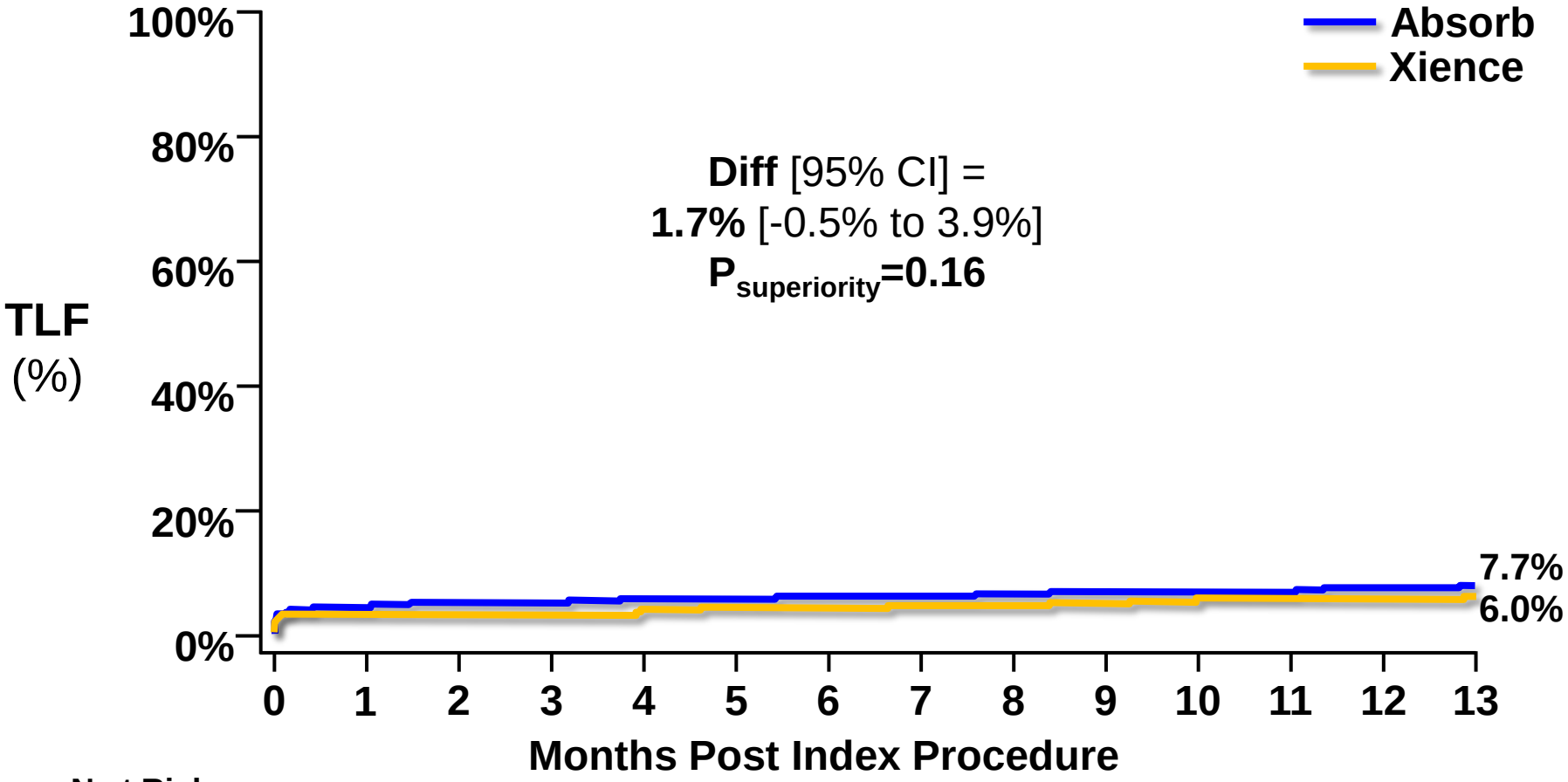
Non-inferiority for 1-Year TLF Also Met in As-Treated Population

As-Treated Population	n / N	%	Difference (95% CI)	P_{NI}
Absorb	99 / 1245	8.0	1.9 (-0.4, 4.1)	0.01
Xience	44 / 726	6.1		



Ellis SG et al. N Engl J Med. 2015;373:1905-15

ABSORB III Met Primary Endpoint: Non-Inferior to Xience in 1-Year TLF (ITT)

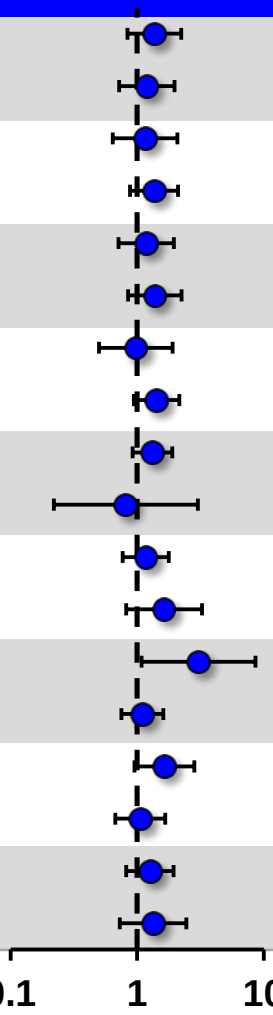


N at Risk					
Absorb	1322	1254	1230	1218	1205
Xience	686	661	651	643	638

Adapted from Ellis SG et al. N Engl J Med. 2015;373:1905-15

No Statistically Significant Interactions in TLF Across All Subgroups (ITT)

Subgroup	Absorb N=1313	Xience N=677	Relative Risk (95% CI)	p-value (interaction)
Age ≥64	8.1%	5.9%	**1.37** (0.84-2.23)	**0.69**
Age <64	7.4%	6.2%	**1.19** (0.72-1.97)	
Female	8.5%	7.4%	**1.16** (0.64-2.08)	**0.68**
Male	7.4%	5.5%	**1.36** (0.88-2.10)	
Diabetes	10.7%	9.1%	**1.18** (0.71-1.95)	**0.68**
No Diabetes	6.3%	4.6%	**1.38** (0.85-2.24)	
Unstable Angina/Recent MI	6.5%	6.6%	**0.98** (0.50-1.90)	**0.35**
Stable CAD	8.3%	5.8%	**1.42** (0.94-2.15)	
Single Lesion Treated	7.7%	5.8%	**1.32** (0.92-1.89)	**0.50**
Dual Lesion Treated	9.4%	11.5%	**0.81** (0.22-3.01)	
Clopidogrel	8.0%	6.8%	**1.17** (0.77-1.78)	**0.43**
Prasugrel or Ticagrelor	7.1%	4.3%	**1.63** (0.82-3.25)	
ACC/AHA Class A or B1	6.8%	2.2%	**3.05** (1.08-8.60)	**0.07**
ACC/AHA Class B2 or C	8.2%	7.5%	**1.10** (0.75-1.61)	
Lesion Length < 11.75 mm	7.9%	4.8%	**1.64** (0.95-2.83)	**0.23**
Lesion Length ≥ 11.75 mm	7.7%	7.3%	**1.06** (0.67-1.67)	
Vessel Diameter < 2.63 mm	9.8%	7.8%	**1.27** (0.82-1.94)	**0.90**
Vessel Diameter ≥ 2.63 mm	5.7%	4.3%	**1.34** (0.73-2.44)	



Ellis SG et al. N Engl J Med. 2015;373:1905-15

Components of the Primary Endpoint (ITT): Hierarchical

	Absorb N=1313 %	Xience N=677 %	p-value (difference)
Target Lesion Failure	**7.8**	**6.1**	**0.16**
Cardiac Death	**0.6**	**0.1**	**0.29**
TV-MI	**6.0**	**4.6**	**0.18**
ID-TLR	**1.1**	**1.3**	**0.72**

TV-MI = target vessel myocardial infarction; ID-TLR = ischemia-driven target lesion revascularization

Ellis SG et al. N Engl J Med. 2015;373:1905-15

Components of the Primary Endpoint (ITT): Non-hierarchical

	Absorb N=1313 %	Xience N=677 %	p-value (difference)
Target Lesion Failure	**7.8**	**6.1**	**0.16**
Cardiac Death	**0.6**	**0.1**	**0.29**
TV-MI	**6.0**	**4.6**	**0.18**
ID-TLR	**3.0**	**2.5**	**0.50**

TV-MI = target vessel myocardial infarction; ID-TLR = ischemia-driven target lesion revascularization

Ellis SG et al. N Engl J Med. 2015;373:1905-15

Peri-Procedural MI Similar in Both Groups (ITT)

CK-MB	Absorb N=1313 %	Xience N=677 %	Difference	p-value
>3x ULN	6.8	6.6	0.2	0.89
>5x ULN (per protocol)	3.0	2.8	0.3	0.75
>8x ULN	1.3	1.3	0.0	0.96
>10x ULN	0.9	1.2	-0.3	0.58
CK-MB > 10x ULN or 5x ULN with Q waves[1]	0.9	1.2	-0.3	0.58

1. SCAI Definition of Clinically Relevant MI. Moussa et al. JACC 2013;62:1563-70
Ellis SG et al. N Engl J Med. 2015;373:1905-15

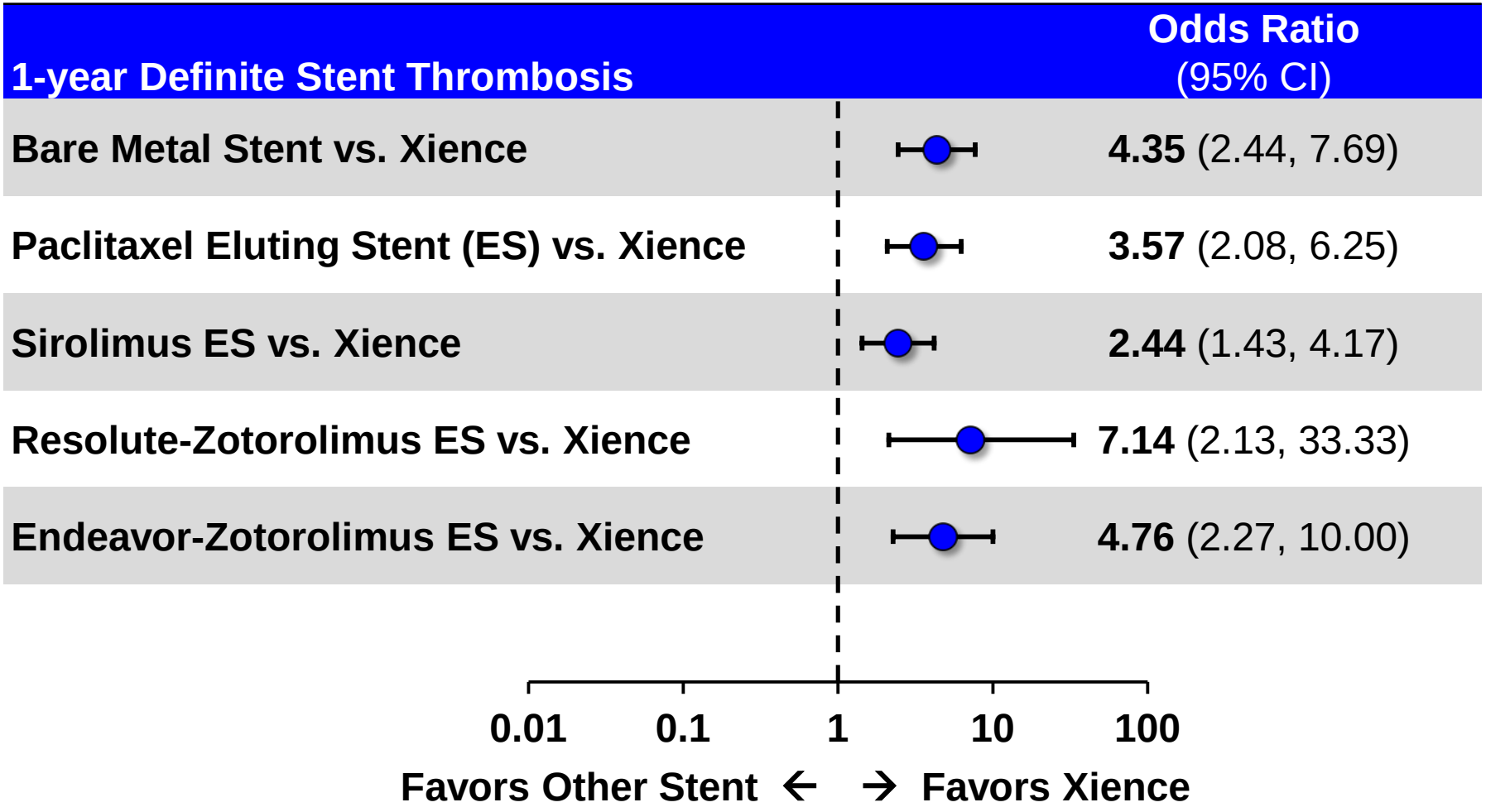
Stent/Scaffold Thrombosis (ITT)

Cumulative Through 1 Year	Absorb N=1313 %	Xience N=677 %	p-value
Definite/Probable	1.54	0.74	0.13
0-30 days (early)*	1.06	0.73	0.46
>30 days - 1 year (late)	0.46	0.00	0.10
Definite*	1.38	0.74	0.21
Probable	0.15	0.00	0.55

*One early definite ST by ITT in Absorb arm was from implanted Xience stent

Ellis SG et al. N Engl J Med. 2015;373:1905-15

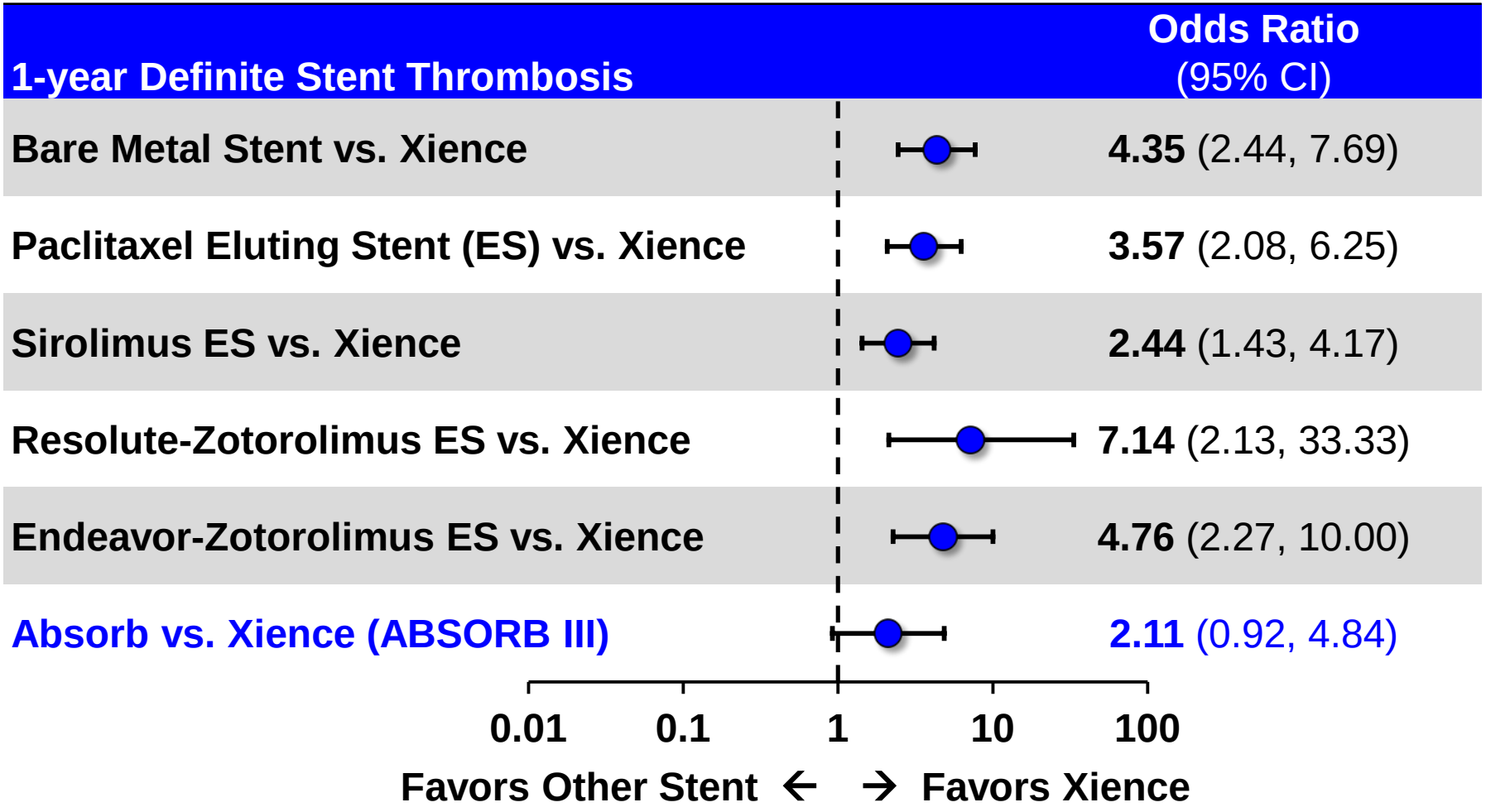
Stent Thrombosis Network Meta-Analysis (49 RCTs; 50,844 Patients)



Data/analysis not submitted or reviewed by FDA

Palmerini T et al. Lancet 2012;379:1393-402

Stent Thrombosis Network Meta-Analysis (49 RCTs; 50,844 Patients) + ABSORB III



Data/analysis not submitted or reviewed by FDA

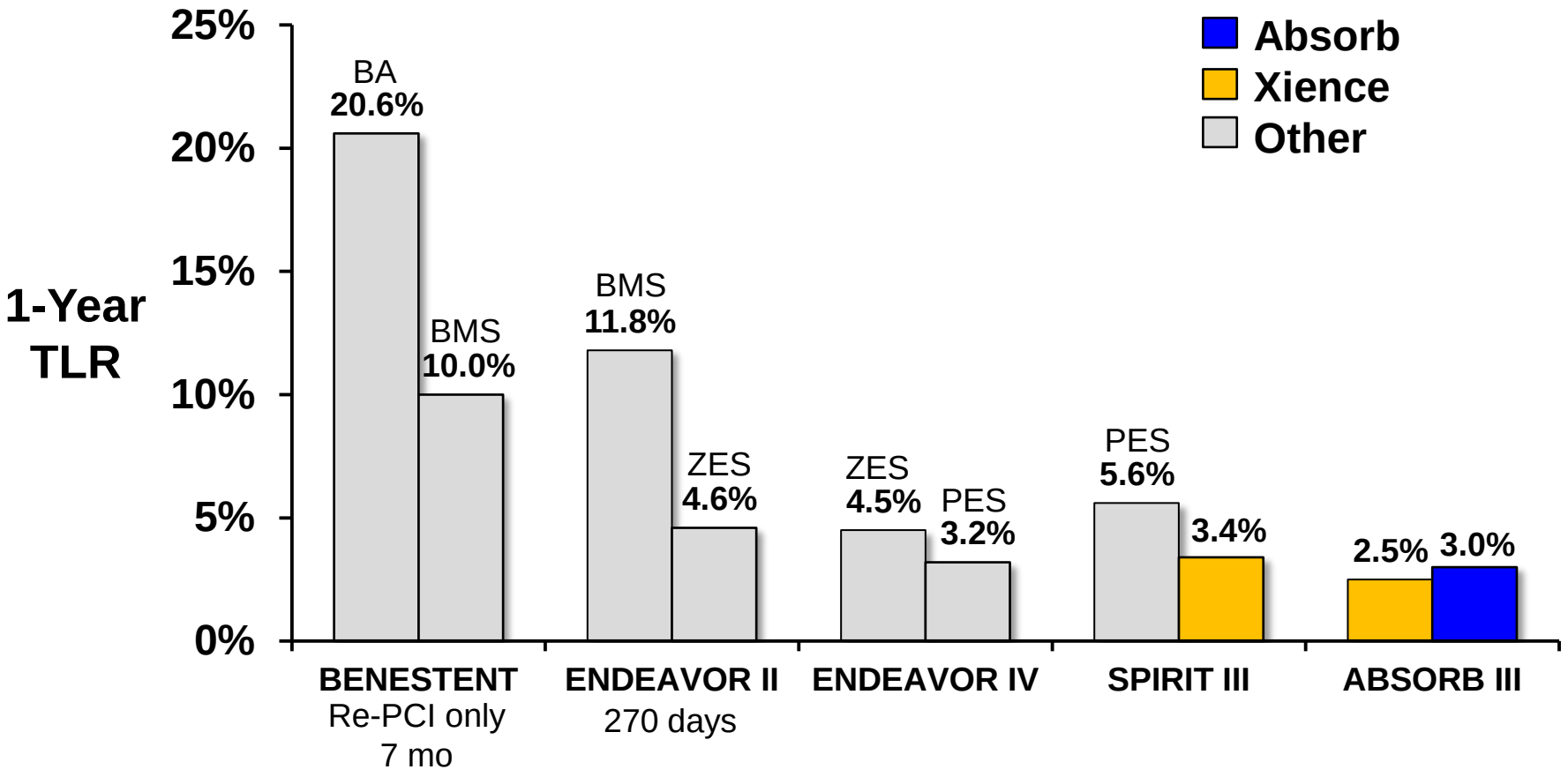
Palmerini T et al. Lancet 2012;379:1393-402

Powered Secondary Endpoints: 1-Year Revascularization and Angina

ITT Population	Absorb N=1313 %	Xience N=677 %	p-value
Angina	18.3	18.4	0.93
All Revascularization	9.1	8.1	---
ID-TVR	5.0	3.7	---

ID-TVR = ischemia-driven target vessel revascularization; Ellis SG et al. N Engl J Med. 2015;373:1905-15

Efficacy of Absorb Preserves DES Treatment Effect



Data/analysis not submitted or reviewed by FDA

Serruys et al. NEJM 1994; Fajadet et al. Circulation 2006; Leon et al. JACC 2010; Stone et al. JAMA 2008

BA: balloon angioplasty; BMS: bare metal stents; ZES: zotarolimus eluting stent; PES: paclitaxel eluting stents; EES: everolimus eluting stents; BVS: Absorb bioresorbable vascular scaffold

ABSORB III Summary: Safety and Effectiveness

- **Absorb met pre-specified criteria for non-inferiority vs. Xience for TLF at 1 year**
- **There were no significant 1-year differences between Absorb and Xience in the safety endpoints of:**
  - All-cause or cardiac mortality
  - Peri-procedural MI, TV-MI or all MI
  - Device thrombosis
- **Absorb was highly effective, with similar rates of ID-TLR as Xience**

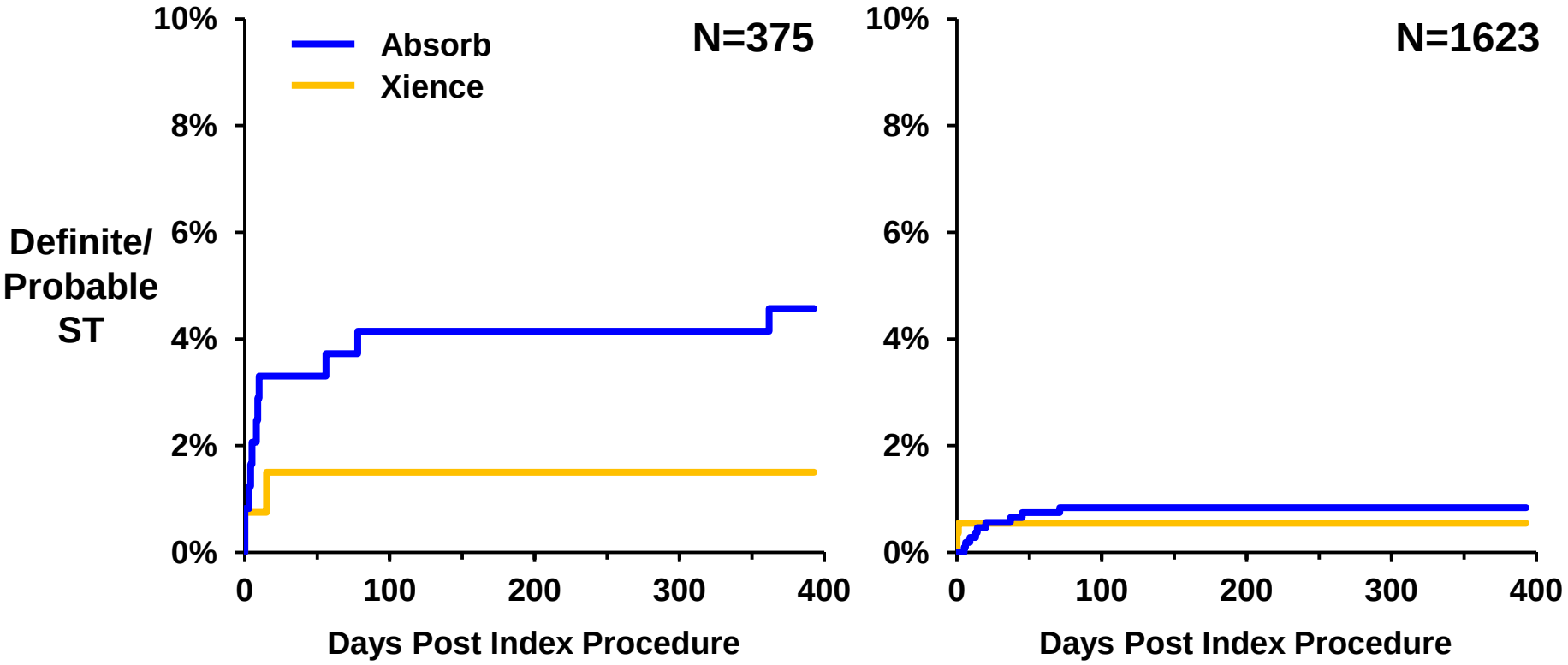
Outcomes by Vessel Size

- At the request of FDA, we performed additional analyses to identify possible correlates of the non-significant difference in device thrombosis
- Given the thicker struts of Absorb, a biologically relevant analysis was to examine outcomes in smaller vessels
- The smallest vessel diameter intended for inclusion in ABSORB III was 2.5 mm by visual assessment, which correlates with a reference vessel diameter (RVD) of ~2.25 mm by QCA

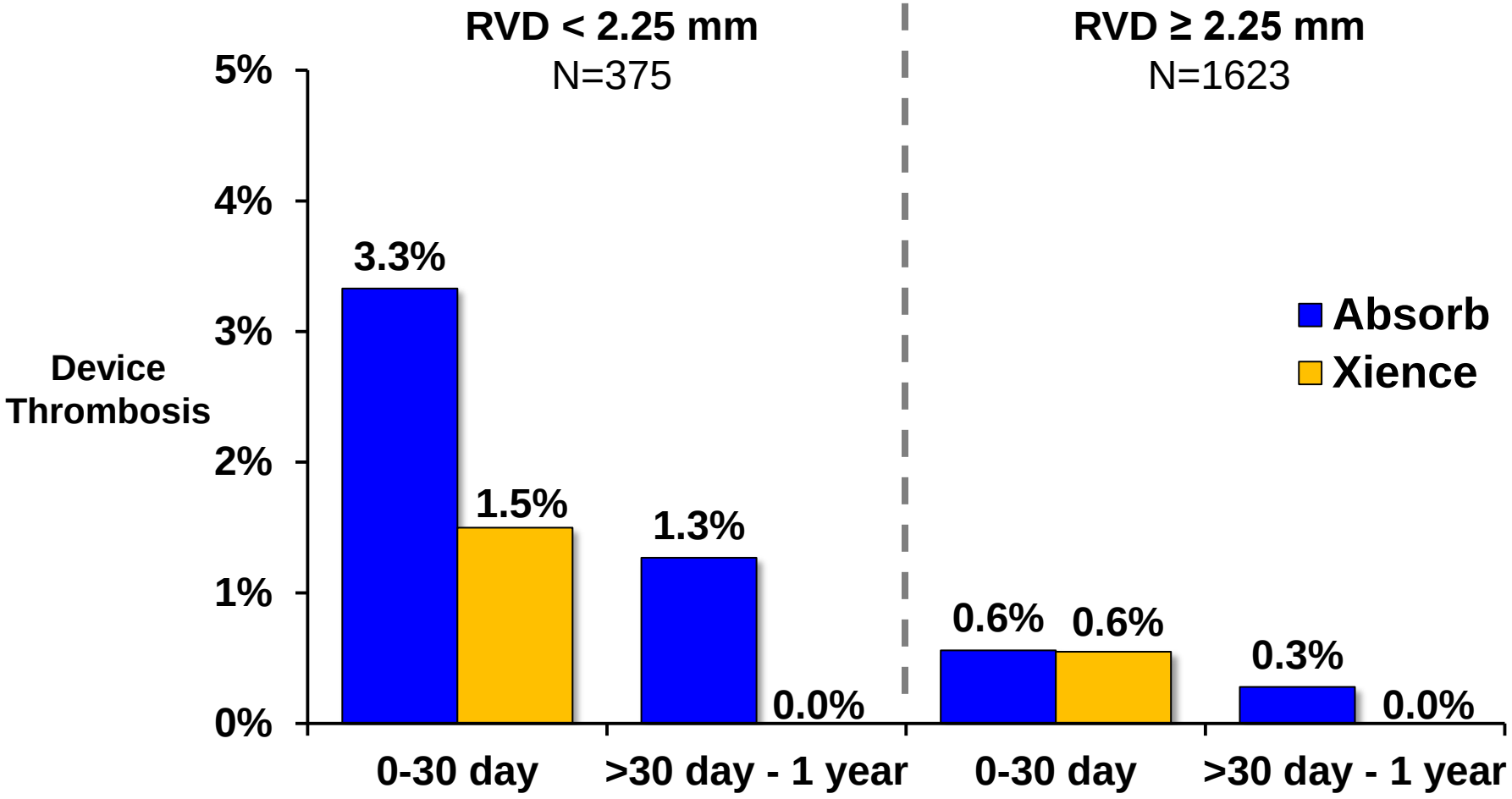
1-Year Device Thrombosis by Vessel Size: Any RVD < 2.25 mm vs. all RVD ≥ 2.25 mm

Any RVD < 2.25 mm
4.6% (Absorb) vs. 1.5% (Xience)
Diff [95%CI] = 3.1 [-0.3, 6.4]

All RVD ≥ 2.25 mm
0.8% (Absorb) vs. 0.5% (Xience)
Diff [95%CI] = 0.3 [-0.5, 1.1]



Device Thrombosis by Timing and Vessel Size

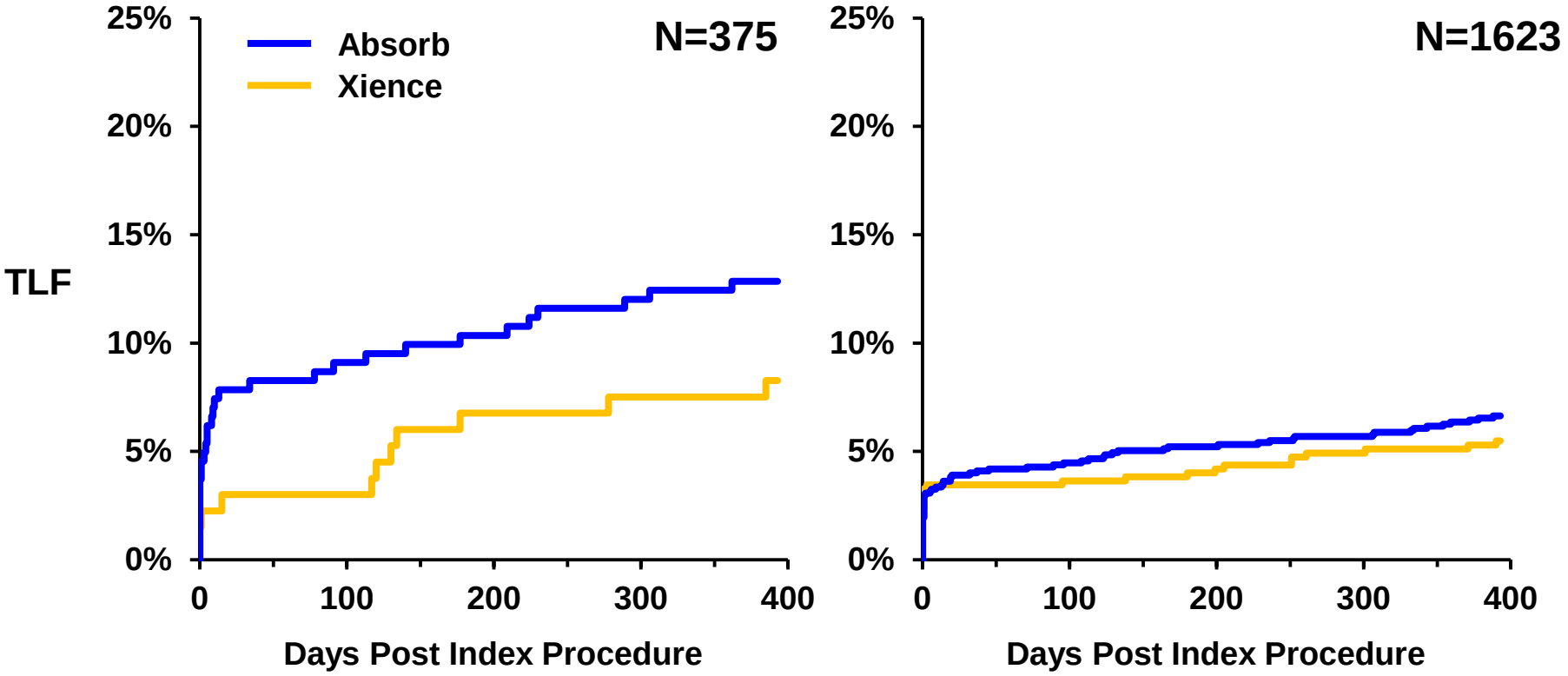


Data/analysis not submitted or reviewed by FDA

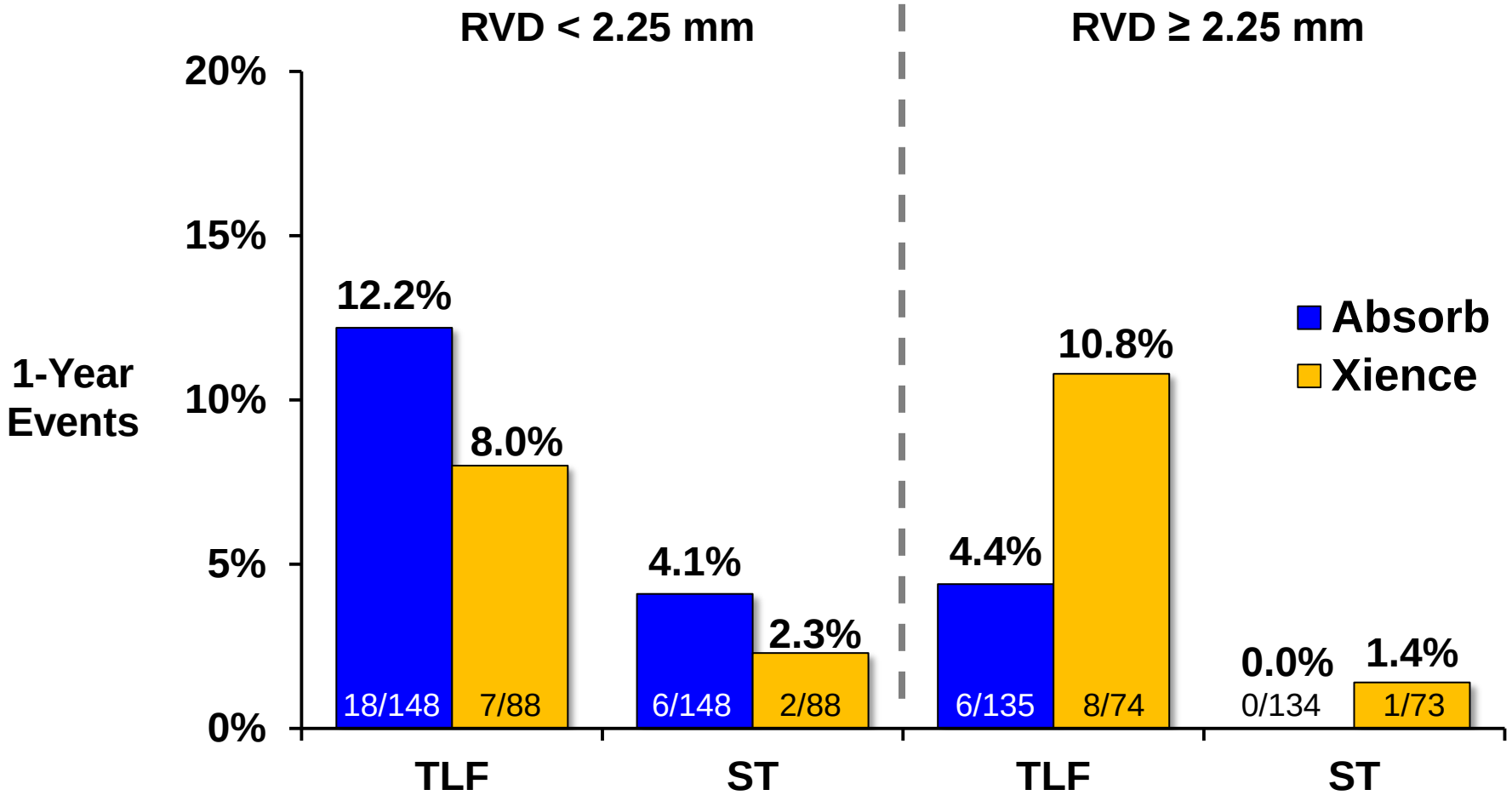
1-Year TLF by Vessel Size: Any RVD < 2.25 mm vs. All RVD ≥ 2.25 mm

Any RVD < 2.25 mm
12.9% (Absorb) vs. 8.3% (Xience)
Diff [95%CI] = 4.6 [-1.7, 10.9]

All RVD ≥ 2.25 mm
6.6% (Absorb) vs. 5.5% (Xience)
Diff [95%CI] = 1.2 [-1.3, 3.6]

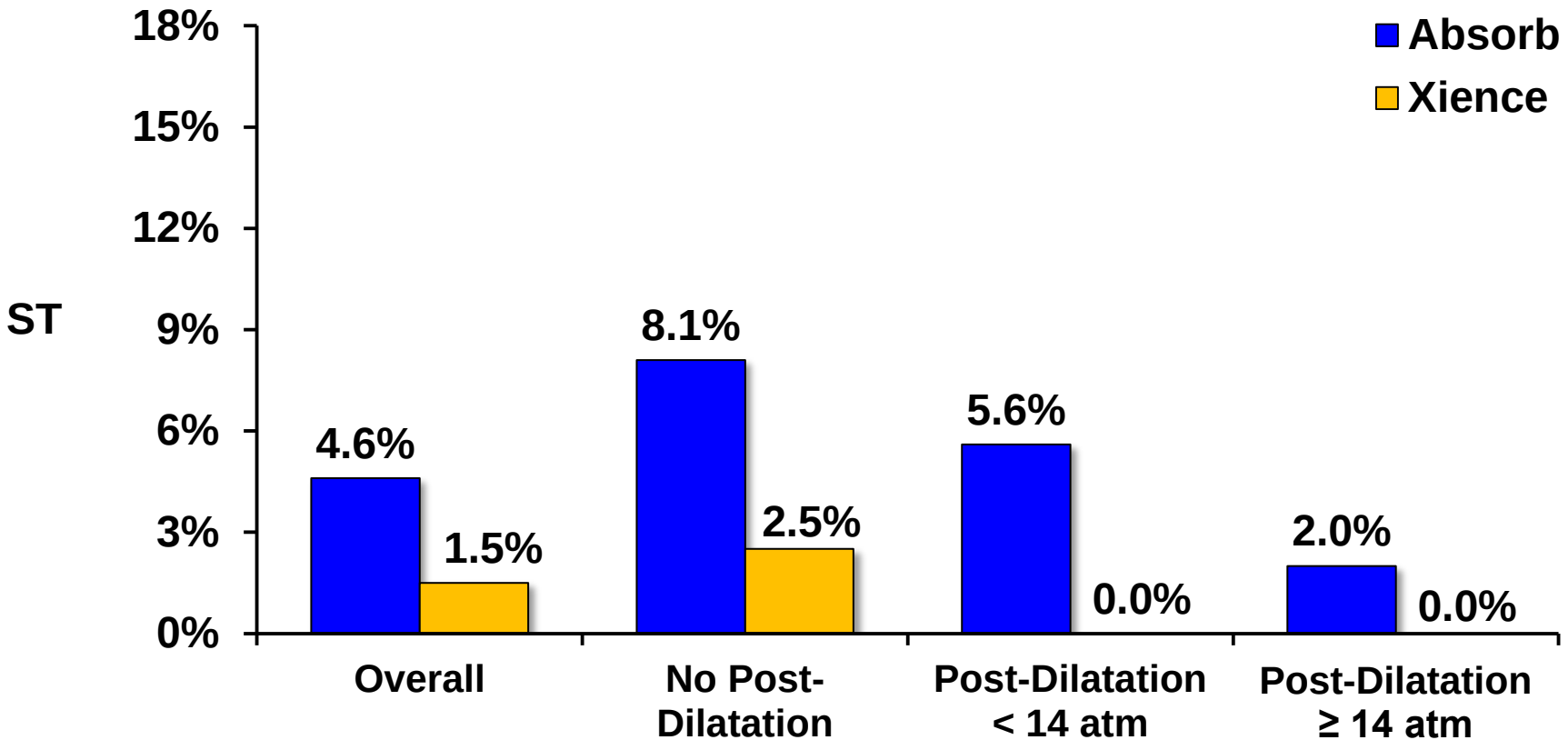


Events by QCA RVD (2.5 mm Device Only, As-Treated Population)



Data/analysis not submitted or reviewed by FDA

Impact of Post-Dilatation and Pressure in Small Vessels (< 2.25 mm) on 1-Year ST



Absorb (n / N)	11 / 238	6 / 74	3 / 54	2 / 101
Xience (n / N)	2 / 133	2 / 79	0 / 15	0 / 36

ABSORB III Diabetic: Overall and Stratified by RVD

1-Year Data	Overall DM		< 2.25 mm		≥ 2.25 mm	
	Absorb N=416	Xience N=224	Absorb N=88	Xience N=45	Absorb N=325	Xience N=177
TLF	10.7%	9.1%	23.9%	15.6%	7.2%	7.5%
Cardiac Death	0.5%	0.0%	1.1%	0.0%	0.3%	0.0%
TV-MI	9.0%	7.3%	19.3%	8.9%	6.2%	6.9%
ID-TLR	5.6%	3.6%	13.6%	13.3%	3.4%	1.1%
ST (def/prob)	3.2%	1.4%	10.6%	4.4%	1.3%	0.6%

- No significant p-values

Primary Endpoint Results (RVD ≥ 2.25 mm)

RVD ≥ 2.25 mm	Absorb N=1074	Xience N=549	Difference [95% CI]	p-value
TLF	6.7%	5.5%	1.1%[1] [-1.5%, 3.4%]	0.38
Cardiac Death	0.6%	0.2%	0.4% [-0.5%, 1.1%]	0.43
TV-MI	5.2%	4.6%	0.5%[2] [-1.9%, 2.6%]	0.64
ID-TLR	2.2%	1.5%	0.8%[3] [-0.8%, 2.1%]	0.29
ST (def/prob)	0.9%	0.6%	0.3% [-0.8%, 1.1%]	0.76

1. Absorb = 6.65%, Xience = 5.54%, difference = 1.12%
2. Absorb = 5.15%; Xience = 4.61%, difference = 0.54%
3. Absorb = 2.249%; Xience = 1.476%, difference = 0.773%

ABSORB III Summary: Vessel Size Considerations

- Compared to the thin strut Xience metallic DES, the thicker strut Absorb had similar outcomes in coronary arteries with QCA RVD ≥ 2.25 mm (those intended for treatment, including diabetic patients)
- In contrast, 1 year event rates with Absorb may be higher in truly very small vessels

ABSORB III Trial: Conclusions

- **Primary endpoint was met:** Absorb was non-inferior to Xience for the composite safety and effectiveness endpoint of TLF at 1 year in ITT study population
- These results improved further when Absorb was used in appropriately sized vessels

ABSORB III Trial: Perspectives

- The 1-year results with this first-in-class device may be enhanced by better operator technique (e.g.,appropriate lesion preparation, device sizing, more frequent post-dilatation, use of intravascular imaging, etc.), the importance of which only became evident after trial enrollment
- The comparable overall outcomes between Absorb and Xience at 1 year sets the stage for the benefits of Absorb in restoring normal coronary physiology and adaptive vascular responses to translate into improved long-term clinical outcomes, a hypothesis being tested in the ABSORB IV trial (results expected in 2020)

Absorb Long-term Data

Absorb Long-Term Clinical Outcomes

- Absorb studies with 2-year follow-up
  - ABSORB Cohort B
  - ABSORB EXTEND
  - ABSORB II
- Absorb studies with longer follow-up
  - ABSORB EXTEND - 3 years
  - ABSORB Cohort B - 5 years

FDA has reviewed Cohort B data through 5 years

FDA has not reviewed EXTEND data beyond 2 years

Studies with Complete 2-Year Absorb Data

N=Absorb Patients	ABSORB Cohort B N=101	ABSORB EXTEND N=812	ABSORB II N=335
N (1 year)	101	811	329
N (2 year)	100	807	328
# of Sites	12	56	46
Treatment	Up to 2 *de novo* lesions in different epicardial vessels		
Trial Oversight	CEC; DSMB; Core Lab for Angio, IVUS, and OCT; Monitoring		

Data/analysis not submitted or reviewed by FDA

Approximate 2% Increment in TLF in Absorb from 1 to 2 Years

Study	N	Year 1	Year 2	Difference [95% CI]
Cohort B	101	6.9%	9.0%	**2.1%** [-5.41, 9.55]
ABSORB Extend	812	5.1%	6.9%	**1.9%** [-0.43, 4.20]
ABSORB II	335	4.8%	7.0%	**2.2%** [-1.42, 5.78]
Pooled	1248	5.1%	7.1%	**2.0%** [0.09, 3.87]
SPIRIT III (Xience)	669	5.5%	7.5%	**2.0%** [-0.69, 4.66]

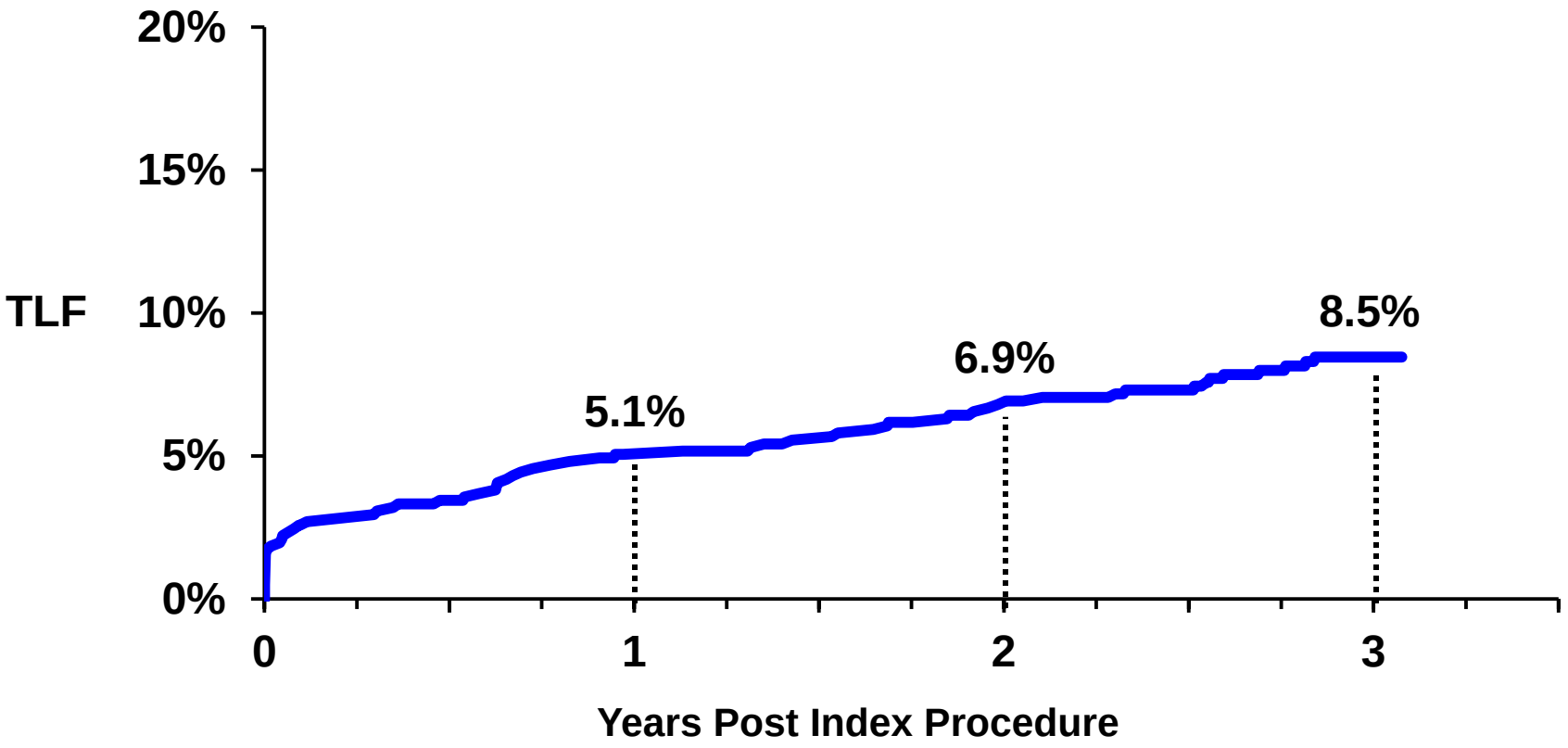
Data/analysis not submitted or reviewed by FDA

Approximate 0.5% Increment in ST (Def/Prob) in Absorb from 1 to 2 Years

Study	N	Year 1	Year 2	Difference [95% CI]
Cohort B	101	0.0%	0.0%	**0.0%** [0.00, 0.00]
ABSORB Extend	812	1.0%	1.5%	**0.5%** [-0.57, 1.60]
ABSORB II	335	0.9%	1.5%	**0.6%** [-1.06, 2.31]
Pooled	1248	0.9%	1.4%	**0.5%** [-0.34, 1.34]
SPIRIT III (Xience)	669	0.9%	1.3%	**0.4%** [-0.80, 1.49]

Data/analysis not submitted or reviewed by FDA

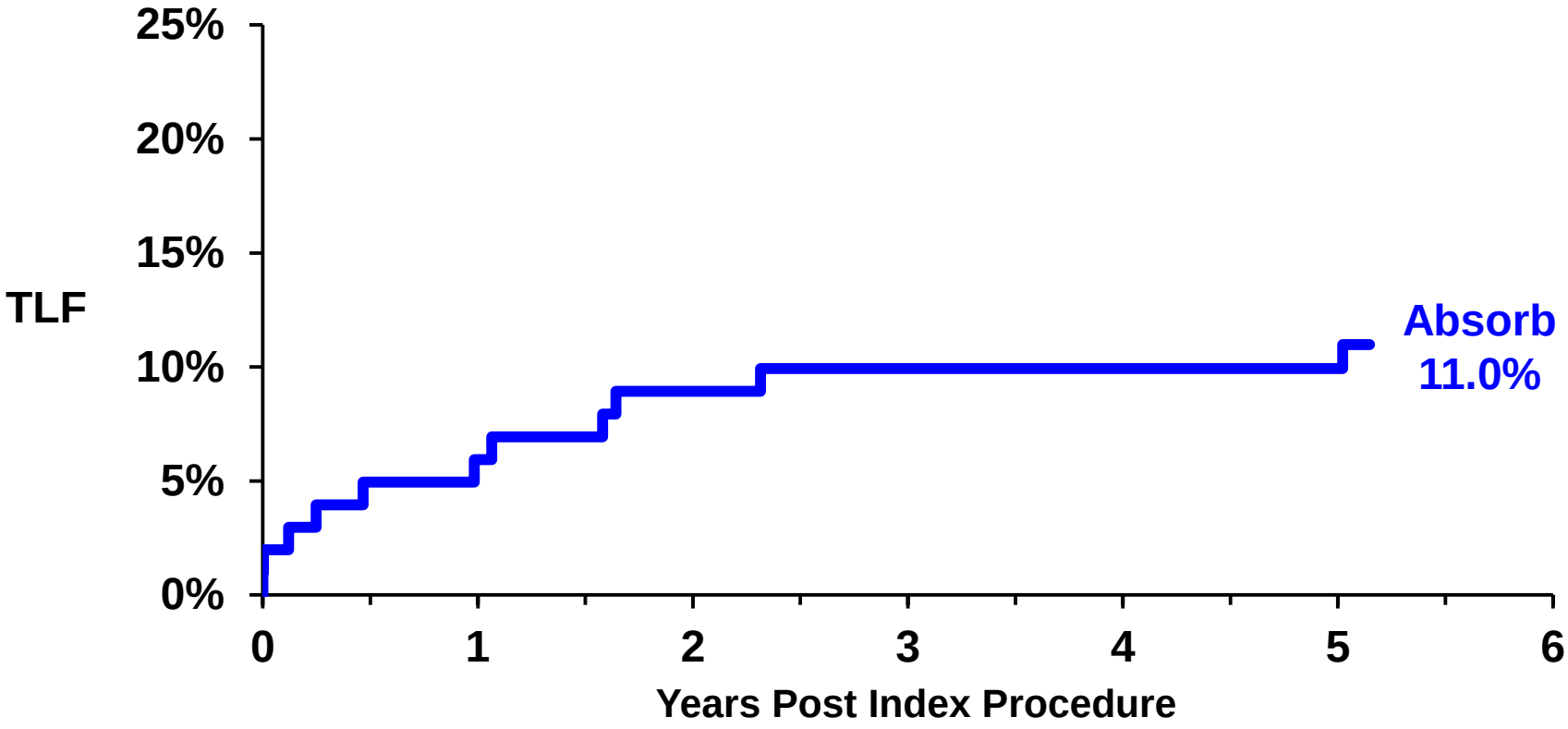
Absorb EXTEND Data Beyond 2 Years



N at Risk				
Absorb	812	766	740	566

Data/analysis not submitted or reviewed by FDA

Absorb Cohort B through 5 Years



N at Risk						
Absorb	101	94	91	88	86	85

Cohorts B1 and B2; Scaffold size: 3.0x18 mm

Adapted from Serruys et al. J Am Coll Cardiol 2016;67:766–76

ABSORB Cohort B: 5 Year Clinical Data

	1 Year N=101 %	2 Years N=100 %	3 Years N=100 %	4 Years N=100 %	5 Years N=100 %
TLF	6.9	9.0	10.0	10.0	11.0
Cardiac Death	0.0	0.0	0.0	0.0	0.0
TV-MI	3.0	3.0	3.0	3.0	3.0
ID-TLR	4.0	6.0	7.0	7.0	8.0
ST (ARC def/prob)	0.0	0.0	0.0	0.0	0.0

Serruys et al. J Am Coll Cardiol 2016;67:766–76

Conclusion: Absorb Events Similar to Xience from 1 to 2 Years

- Incremental rates of TLF and ST between 1 and 2 years were low and similar for Absorb and Xience across 3 trials
  - Cohort B, EXTEND, ABSORB II (N=1248)
- Current results suggest that relatively few events accrue in Absorb-treated patients after 2 years

Data/analysis not submitted or reviewed by FDA

High Level Summary: Benefit-Risk Analysis

Conclusions: Safety

- In the present 2,008 patient randomized trial, there were no significant differences in any of the major safety endpoints between Absorb and Xience
  - Despite the fact that most operators had never previously used Absorb
- Absorb and Xience had very similar and low rates of adverse events when used in appropriately sized vessels

Conclusions: Effectiveness

- The rate of ischemic TLR after Absorb was nearly identical to Xience, and was consistent with the expected efficacy from a current generation, potent DES

Conclusions: Balance of Benefit vs. Risk

Benefits:

- Absorb has been demonstrated to be a safe and effective anti-proliferative device for PCI
- These outcomes are achieved with a device that completely resorbs, thus avoiding the chronic issues inherent in a permanent metallic DES, including jailing side branches, eliminating late surgical options, and requiring multiple stent layers

Risks:

- Using Absorb in very small vessels (QCA RVD <2.25 mm)
  - Addressed through appropriate labeling and physician education / training

Sponsor Commitments

Chuck Simonton, MD, FACC, FSCAI

Chief Medical Officer

Divisional Vice President

Abbott Vascular

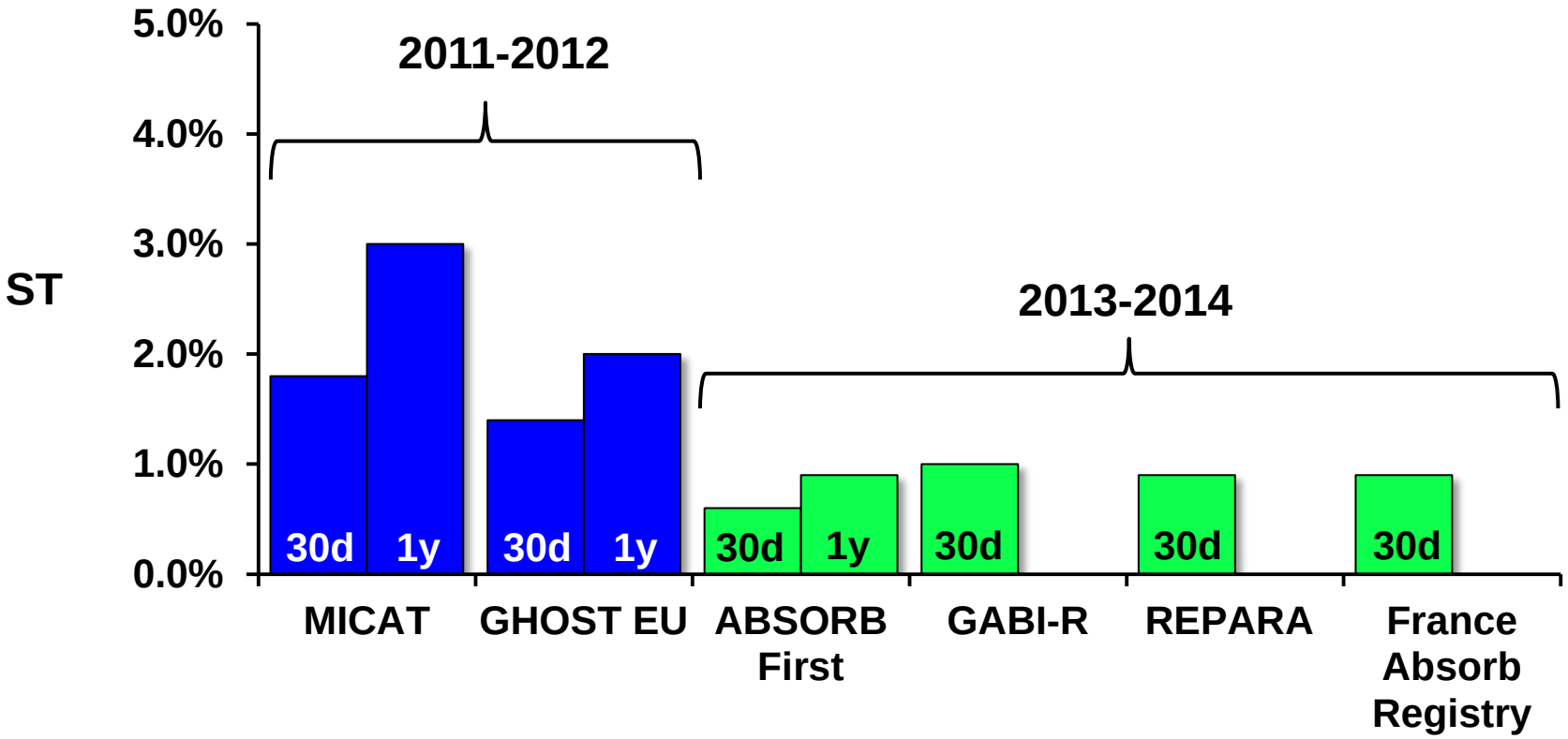
Sponsor Commitments

- Learnings from international experience
- Labeling
- Physician education and training
- Phased commercial launch
- Post-approval study

Optimizing Implant Techniques: International Experience and ABSORB III

- International Experience:
  - Absorb implant procedure fundamentally similar to DES, but with emphasis on:
    - Good lesion preparation
    - Appropriate sizing of scaffold
    - Post-dilatation to full lesion expansion
- Learning from ABSORB III trial:
  - Optimal outcomes in appropriately sized vessels consistent with proposed label

Absorb Scaffold Thrombosis in Real-World Registries of ≥ 1000 Patients

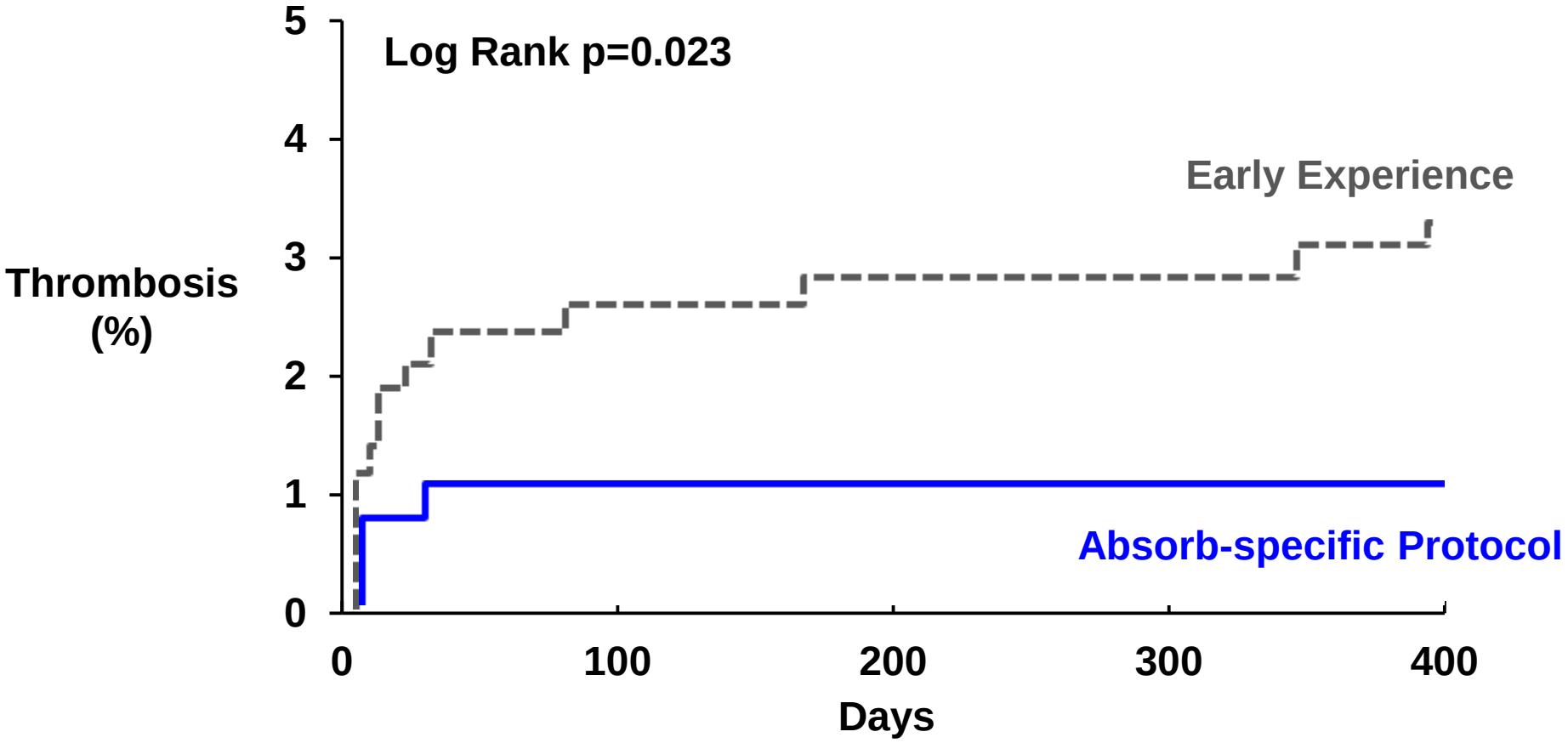


N=	1305	1477	1800	2003	1669	1263

Data/analysis not submitted or reviewed by FDA

Capodanno et al, GHOST-EU Investigators – EuroIntervention 2015;10:1144-53; Puricel, S. et al. J Am Coll Cardiol. 2016; 67(8):921–31; Seth et al. TCT 2015; Hamm EiuroPCR 2015; Koning TCT 2015

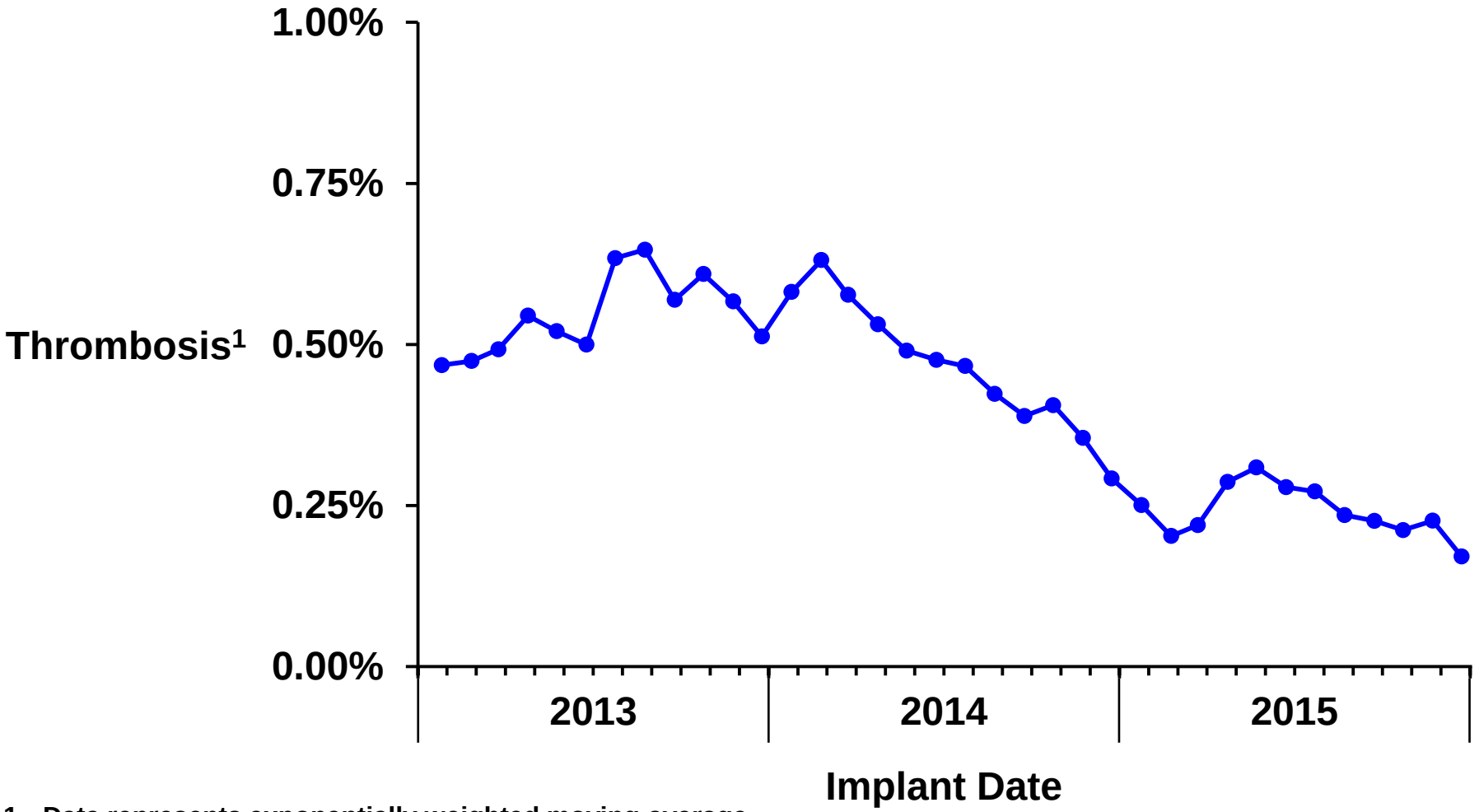
ABSORB Learnings: MICAT



Patients (N)					
Early Experience	369	369	369	369	369
Absorb-specific	292	292	281	217	155

Puricel, S. et l. J Am Coll Cardiol. 2016; 67(8):921–31

Worldwide Absorb Voluntary Reporting of Thrombosis by Implant Date



1. Data represents exponentially weighted moving average

Data/analysis not submitted or reviewed by FDA

Absorb Proposed Labeling

Precaution Statements

- *"In small vessels (visually assessed as ≤ 2.75 mm), on-line QCA or intravascular imaging is strongly recommended to accurately measure and confirm appropriate vessel sizing (≥ 2.5 mm)"*
- *Post-dilatation is strongly recommended for optimal scaffold apposition. When performed, post-dilatation should be at high pressure with a non-compliant balloon.*

Warning Statement

- *"If quantitative imaging determines a vessel size < 2.5 mm, do not implant Absorb. Implantation of the device in vessels < 2.5 mm may lead to an increased risk of adverse events such as myocardial infarction and scaffold thrombosis"*

Mandatory Comprehensive Absorb Education and Training Program

Each physician will complete program before implanting Absorb commercially	
1	**Three Online Training Modules** • Module 1: Overview of device features and design • Module 2: Deployment and implantation technique • Module 3: Case reviews
2	**In-Person Education with Absorb Experts** • Interactive case reviews and discussion • Device overview • Review of clinical data • Patient selection according to label • Deployment and implantation Technique • Review initial case plan
3	**3-5 Monitored Cases (by AV personnel)** • Documentation of patient selection according to label • Angiograms analyzed by core lab QCA for appropriate vessel sizing (first 500 cases)

Phased Commercial Launch

Phase 1

- 100 sites
- 500 patients
- All angiograms analyzed by core lab QCA (education validation)
- Invited to post-approval study

Phase 2

- 150+ sites
- 2000+ patients
- Invited to post-approval study

Phase 3

- 300+ sites
- Continued commercial launch

Proposed Post-Approval Commitments

- All ABSORB III patients will be followed to 5 years
- ABSORB IV has enrolled N=1642 of 3000, followed to 5 years
- First 500 commercial patients will have angiographic baseline analysis (core lab QCA) to ensure appropriate vessel sizing and effectiveness of training
- Post-approval study (PAS) synchronized with commercial launch
  - All commercial sites will be invited to participate in PAS immediately upon launch
  - Up to 5000 patients
  - Approximately 250 sites
  - Ongoing review of clinical outcome data with FDA
  - 5 year follow-up of safety and effectiveness outcomes

Clinical Perspective

Mitchell W. Krucoff, MD

Director, Cardiovascular Devices Unit

Duke Clinical Research Institute

Professor of Medicine, Cardiology

Duke University Medical Center

Absorb GT1™ Bioresorbable Vascular Scaffold (BVS) System

March 15, 2016

Abbott Vascular

Circulatory System Devices Panel