Absorb GT1™ Bioresorbable Vascular Scaffold (BVS) System

FDA Review of P150023

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Center for Devices and Radiological Health
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FDA Presentations

- Introduction and Regulatory History
  Dr. Kenya Brothers
- Statistical Presentation
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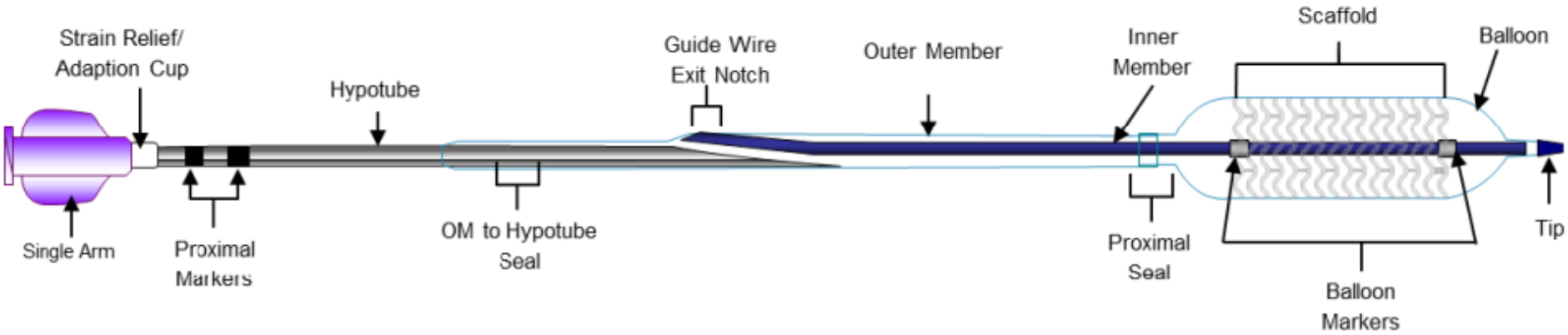
Device Description

- Balloon dilatation catheter (Delivery System)
- Absorbable polymeric (poly(L-lactide), PLLA) scaffold
- Drug-eluting coating
  - Absorbable polymer (poly(D,L-lactide), PDLLA)
  - Anti-proliferative/immunosuppressant drug (everolimus)

Delivery System



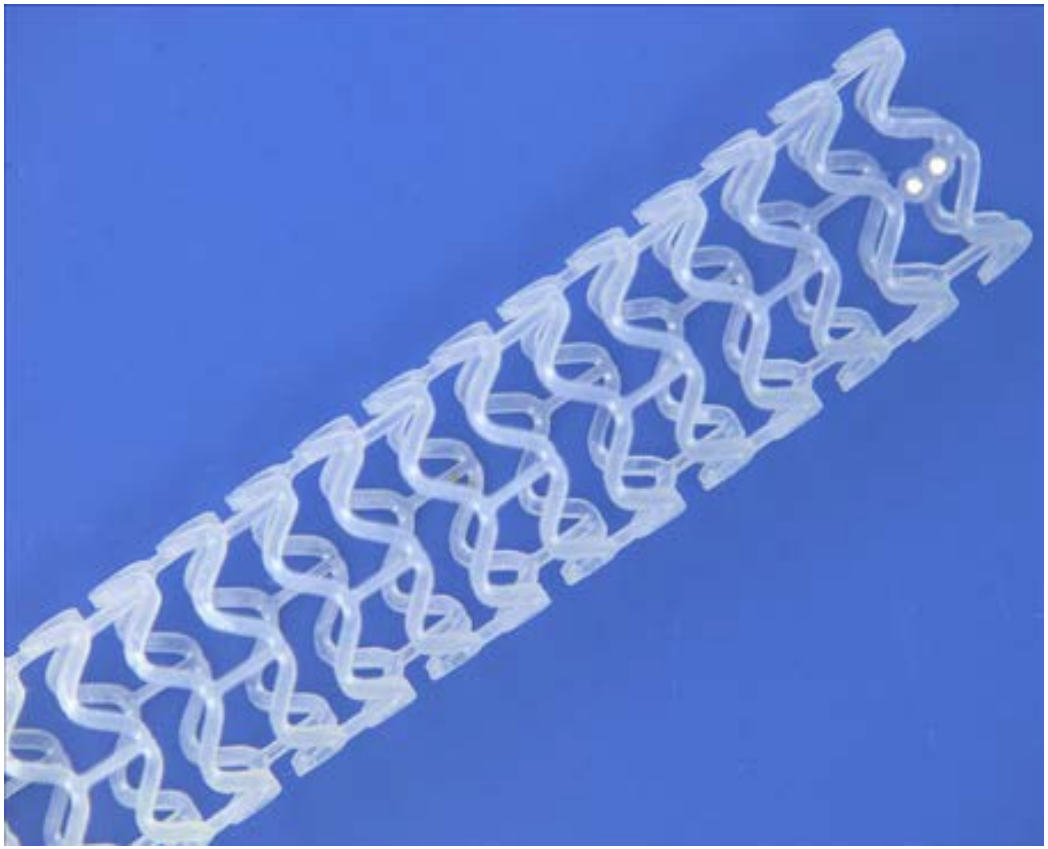
- Delivery system used in ABSORB III RCT slightly different than that proposed in marketing application (Absorb GT1 BVS)
- GT1 delivery system performance assessed via
  - Bench Testing and
  - FDA-approved XIENCE Alpine
- No outstanding issues regarding delivery system – clinical study of Absorb BVS is applicable

BVS Size Matrix

Scaffold Design	Product Diameter (mm)	Product Length (mm)				
		8	12	18	23	28
Small	2.5	X	X	X	X	X
	3.0	X	X	X	X	X
Medium	3.5	N/A	X	X	X	X

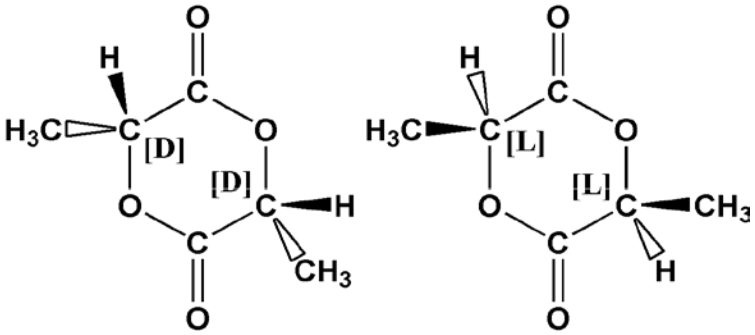
Bioresorbable Vascular Scaffold

- Poly(L-lactide)
- Sinusoidal rings
- Linear links connect rings
- Platinum markers
- Two distinct designs
  - Small (2.5 & 3.0 mm diameters)
  - Medium (3.5 mm diameters)

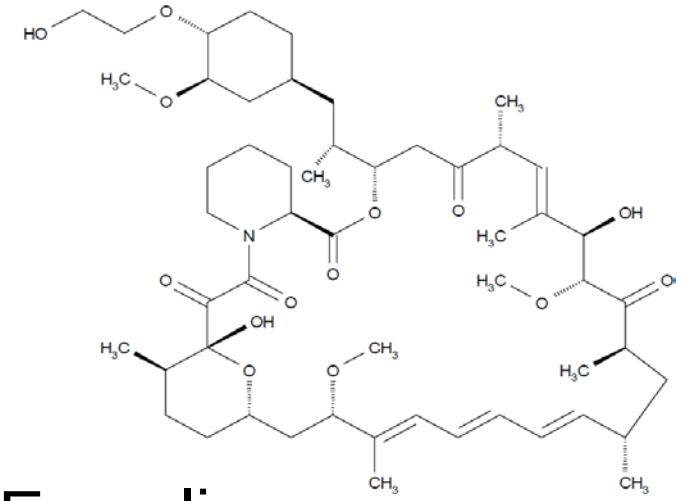


Digital Photograph of the 3.5 mm Medium BVS in Expanded Form

Drug-Eluting Coating



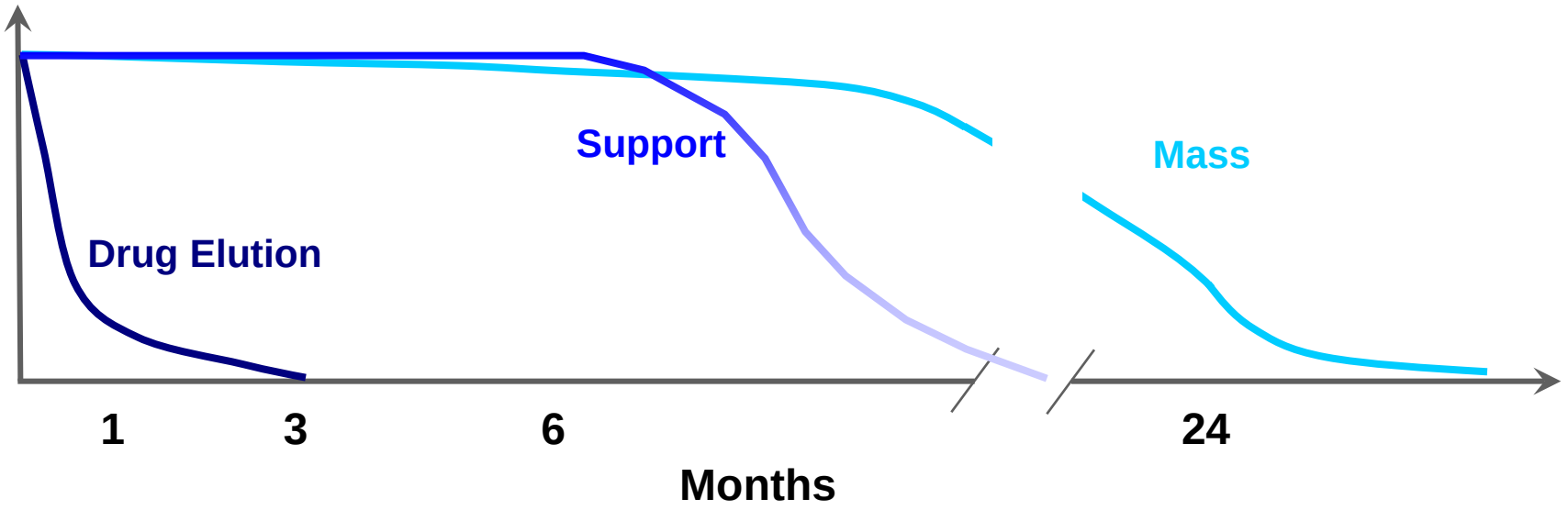
- Poly(D,L-lactide)
- Control drug release



- Everolimus
- Prevent smooth muscle cell proliferation
- Identical drug component in XIENCE

Device Mechanism of Action

Revascularization | **Restoration** | **Resorption**

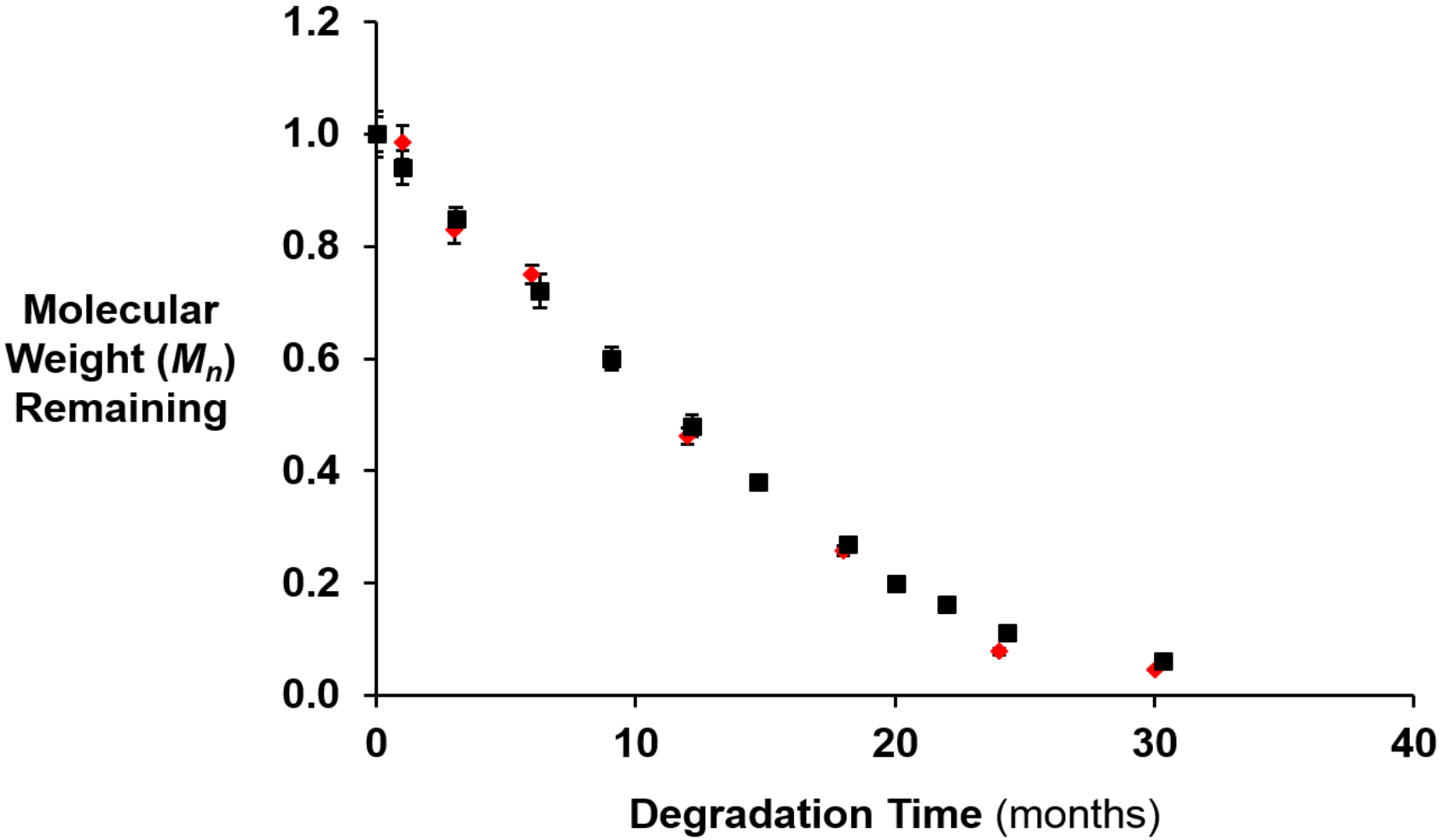


- Provide temporary arterial mechanical support
- Elute antiproliferative drug – prevent restenosis
- Disappear once arterial support no longer needed

Bench Testing

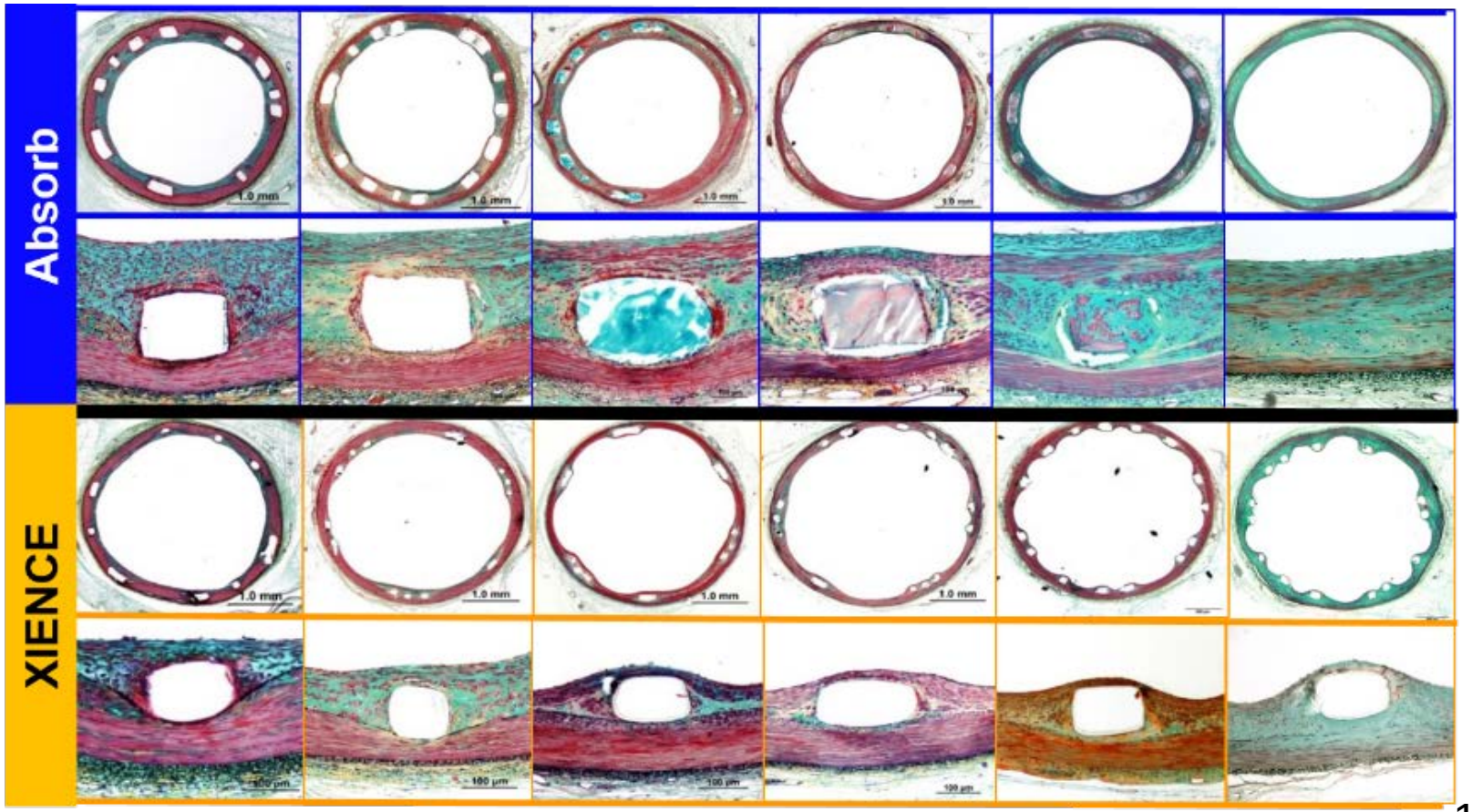
- FDA Guidance
  - *Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*
- Consensus Standards
  - ASTM
  - USP
  - ISO
  - ICH
  - OECD

In Vitro / *In Vivo* Correlation



In vitro **data – n = 6 for all time points**
In vivo **data – n = 8 - 14 for all time points**

In Vivo Vascular Responses



BVS vs. XIENCE

	BVS	XIENCE
Platform	PLLA	Cobalt Chromium
Drug Coating	PDLLA + Everolimus	PVDF-HFP + Everolimus
Strut Thickness	~150µm	~81µm
Strut Width	~200µm	~105µm

Non-Clinical Summary

- BVS performance evaluated on the bench and in a healthy animal model
- BVS undergoes hydrolytic degradation and is absorbed in an *in vivo* animal model
- *In vivo* animal studies showed scaffold reached complete absorption at 36 months
- No outstanding non-clinical issues

Proposed Indications for Use

Indications 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.

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FDA Statistical Review: ABSORB III (P150023) Abbott Vascular

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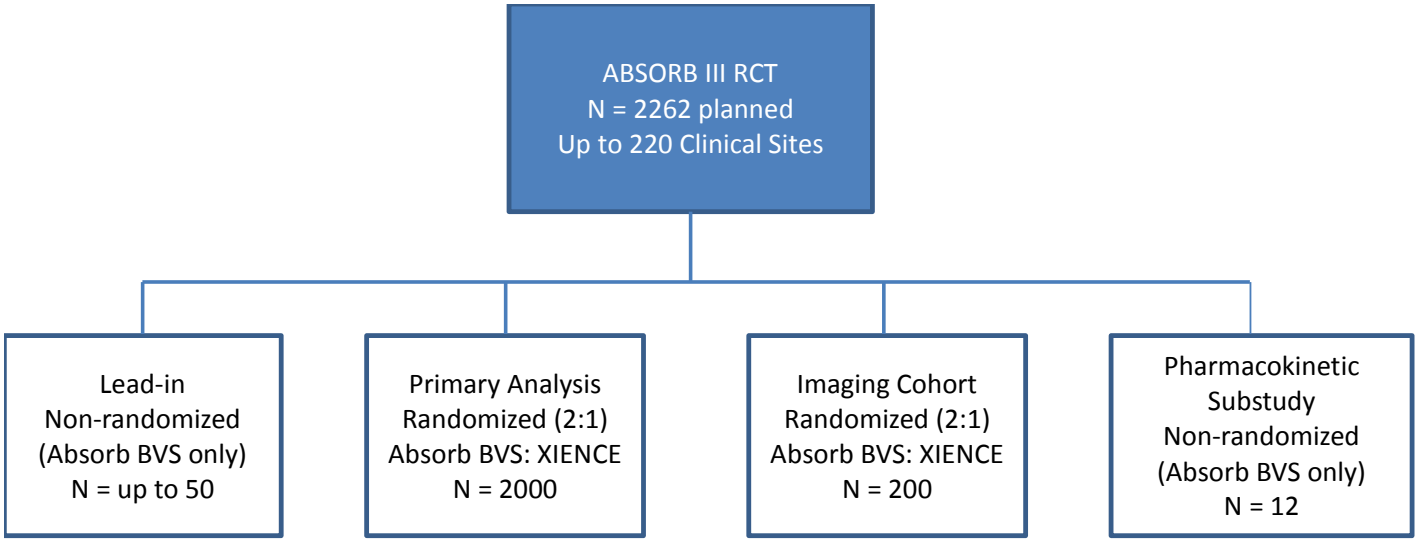
Center for Devices and Radiological Health
CDRH

Outline

- ABSORB III Study Design
- Primary Analysis Group Results at One Year
  - Primary endpoint
  - Secondary endpoints with pre-specified hypothesis tests
- Statistical Summary

ABSORB III Study Design

- ABSORB III includes four sub-studies:



- In the scope of this PMA, the statistical evaluation of the primary and secondary endpoints were based on the Primary Analysis Group

Primary Analysis Group

- Prospective, multi-center, randomized, single-blinded (subject), two-arm trial
  - Investigational device group: BVS
  - Concurrent control group: XIENCE
- 2:1 Randomization (n=2008 randomized)
  - BVS: n=1322
  - XIENCE: n=686

Primary Endpoint

- Target lesion failure (TLF) at 1 year
  - TLF: the composite of cardiac death, myocardial infarction (MI) attributable to target vessel (TV-MI), or ischemia-driven target lesion revascularization (ID-TLR)
  - Pre-specified non-inferiority (NI) test: NI margin=4.5%

$$H_0 : TLF_{BVS} - TLF_{XIENCE} \geq 4.5\%$$

$$H_A : TLF_{BVS} - TLF_{XIENCE} < 4.5\%$$

Secondary Endpoints
with pre-specified hypothesis tests (1)

- Angina at 1 year
  - Defined as the first adverse event resulting in the site diagnosis of angina;
  - Excluding angina following the index procedure through discharge, not to exceed a period of 7 days.
- All revascularization at 1 year
  - Comprised of target lesion revascularization (TLR), target vessel revascularization (TVR) excluding TLR, and non-TVR
- Ischemia-driven target vessel revascularization (ID-TVR) at 1 year

Secondary Endpoints
with pre-specified hypothesis tests (2)

- Pre-specified superiority tests:
  - Angina at 1 year

$$H_0 : ANGINA_{BVS} - ANGINA_{XIENCE} = 0$$
$$H_A : ANGINA_{BVS} - ANGINA_{XIENCE} \neq 0$$

  - All revascularization at 1 year

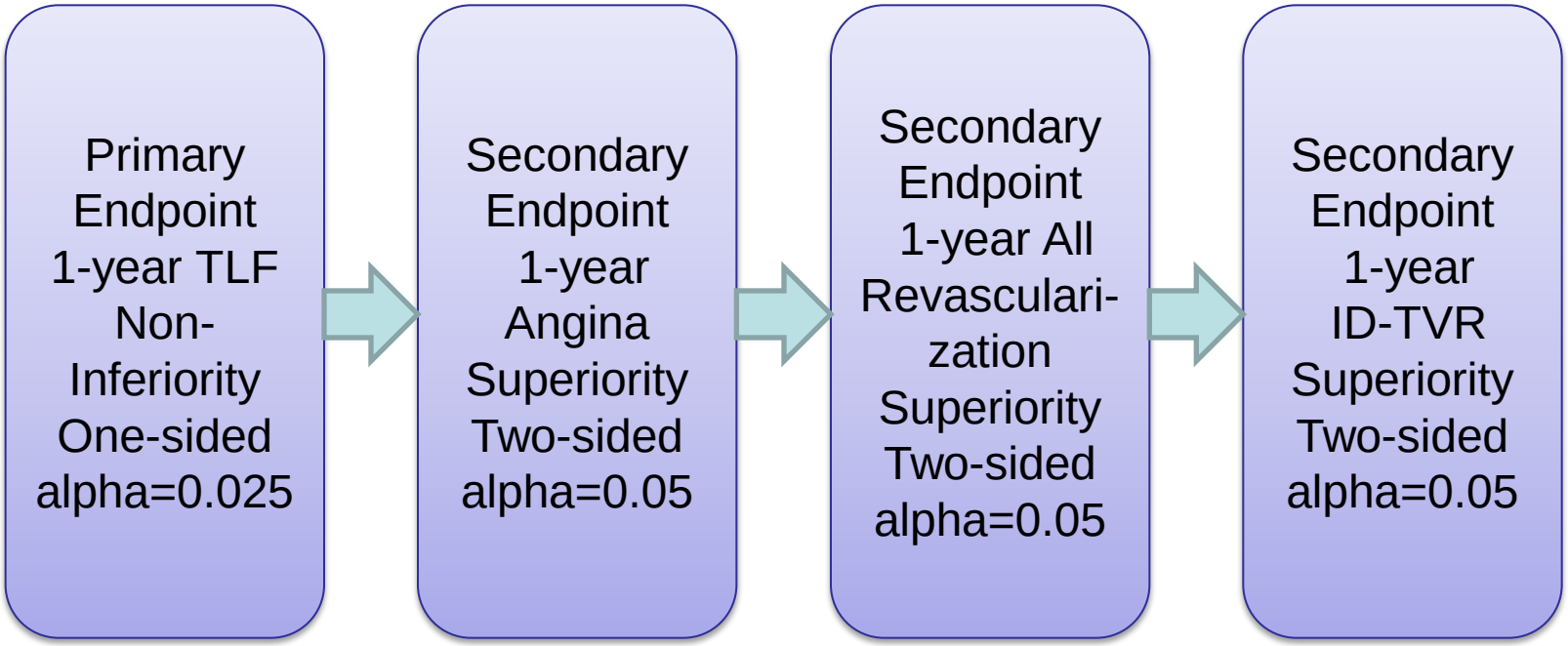
$$H_0 : ALLREVASC_{BVS} - ALLREVASC_{XIENCE} = 0$$
$$H_A : ALLREVASC_{BVS} - ALLREVASC_{XIENCE} \neq 0$$

  - ID-TVR at 1 year

$$H_0 : IDTVR_{BVS} - IDTVR_{XIENCE} = 0$$
$$H_A : IDTVR_{BVS} - IDTVR_{XIENCE} \neq 0$$

Secondary Endpoints
with pre-specified hypothesis tests (3)

- Testing sequence:



Study Success Criterion

- The study will be considered a success when the study meets the primary endpoint of TLF at 1 year.

Analysis Populations (1)

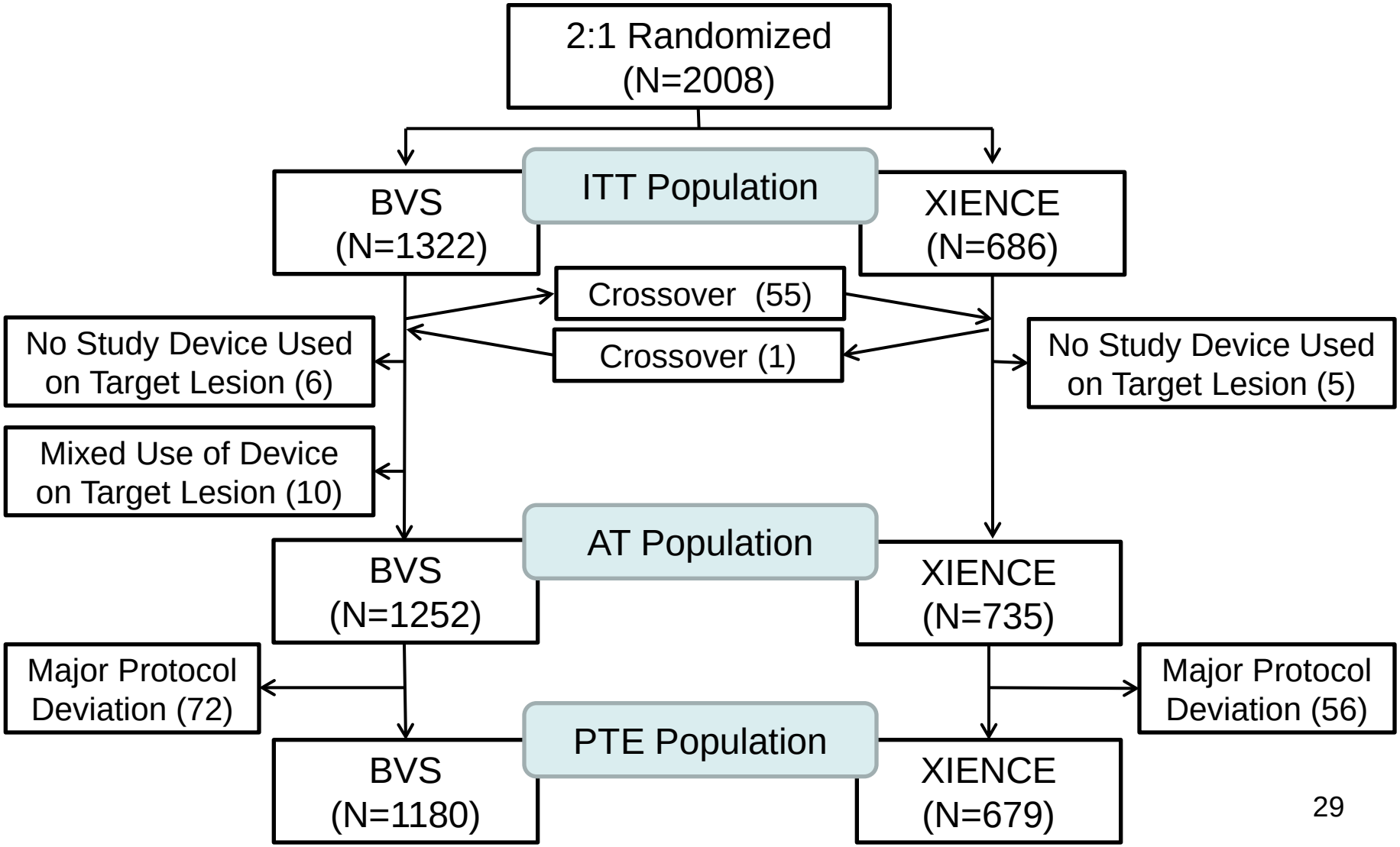
- The Intent-to-Treat (ITT) population
  - Including all randomized subjects
  - Analyzed based on the randomization assignment

- The Per-Treatment-Evaluable (PTE) population
  - Including subjects who have received only study devices (BVS or XIENCE) at the target lesion
  - Excluding subjects with major protocol deviations
  - Analyzed based on the treatment actually received

Analysis Populations (2)

- The As-Treated (AT) population
  - Analyzed based on the treatment actually received
  - Subjects who received both BVS and XIENCE at separate target lesions were analyzed based on the randomization assignment
  - Excluding subjects who received both BVS and XIENCE at the same target lesion
  - Excluding subjects who received no study device at target lesion

Analysis Population Flow Chart



Primary Analysis Group

Results at One Year

Primary Endpoint Result (1)

- ITT population:

	BVS (N=1322)	XIENCE (N=686)	Difference (95%CI)	NI Margin	NI P-Value
1-Year TLF	7.8% (102/1313)	6.1% (41/677)	1.7% (-0.5%, 3.9%)	4.5%	0.0070

  - The BVS group had higher observed 1-year TLF rate compared to the XIENCE group.
  - The non-inferiority objective of the primary endpoint was met based on the ITT population.

Primary Endpoint Result (2)

- PTE population:

	BVS (N=1180)	XIENCE (N=679)	Difference (95%CI)	NI Margin	NI P-Value
1-Year TLF	7.8% (91/1174)	5.7% (38/670)	2.1% (-0.2%, 4.3%)	4.5%	0.0183

  - The BVS group had higher observed 1-year TLF rate compared to the XIENCE group.
  - The non-inferiority objective of the primary endpoint was met based on the PTE population.

Primary Endpoint Result (3)

- AT population (post-hoc):

	BVS (N=1252)	XIENCE (N=735)	Difference (95%CI)	NI Margin	NI P-Value
1-Year TLF	8.0% (99/1245)	6.1% (44/726)	1.9% (-0.4%, 4.1%)	4.5%	0.0113

  - The BVS group had higher observed 1-year TLF rate compared to the XIENCE group.
  - The result of the post-hoc As-Treated analysis supported the non-inferiority of BVS compared to XIENCE in terms of TLF at 1 year.

Secondary Endpoints Results

- ITT population:

	BVS (N=1322)	XIENCE (N=686)	Difference (95%CI)*	P-Value
1-Year Angina	18.3% (238/1303)	18.4% (125/678)	-0.2% (-3.8%, 3.4%)	0.9256
1-Year All Revascularization	9.1% (120/1313)	8.1% (55/677)	1.0% (-1.6%, 3.6%)	NA
1-Year ID-TVR	5.0% (66/1313)	3.7% (25/677)	1.3% (-0.5%, 3.2%)	NA

*Without multiplicity adjustment

  - The study failed to demonstrate superiority of BVS over XIENCE in terms of angina, all revascularization or ID-TVR at 1 year.

Statistical Summary

- The non-inferiority objective of the primary endpoint, TLF at 1 year, was met. Therefore, the study success criterion was met.

- The BVS group had higher observed 1-year TLF rate compared to the XIENCE group.

- The study failed to demonstrate superiority of BVS over XIENCE in terms of angina, all revascularization or ID-TVR at 1 year.

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FDA Clinical Review
Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System

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ABSORB III

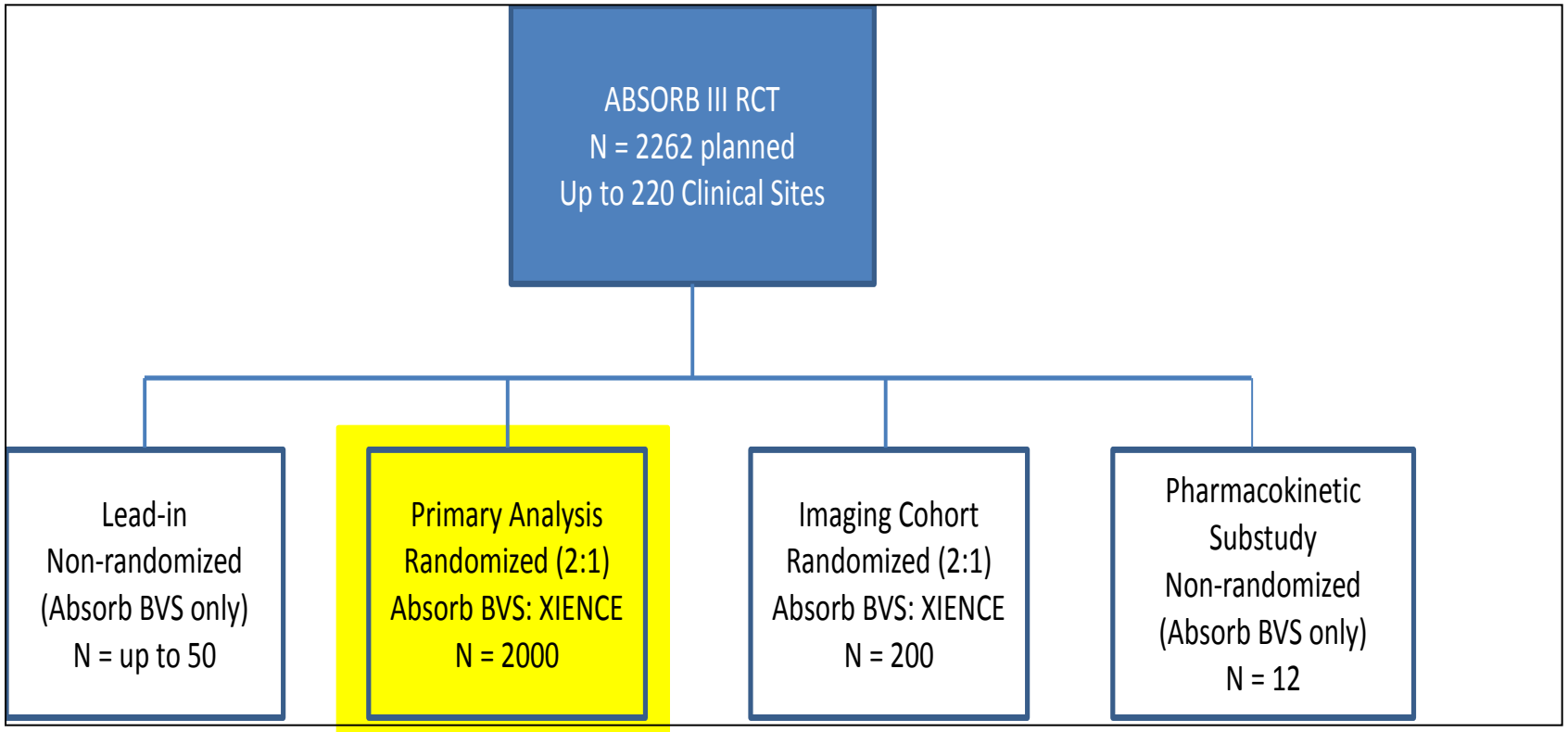
Outline of Clinical Review Presentation

Overview of ABSORB III Trial

- Trial Design
- Study Endpoints
- Inclusion and Exclusion Criteria
- Patient Demographics and Clinical Presentation
- Baseline Lesion Characteristics
- Post Procedure Angiographic Findings

- ABSORB III Safety and Effectiveness Endpoints
- Other ABSORB Studies performed outside the US

ABSORB III Overall Design



ABSORB III RCT

Primary Analysis Group

Study Objective

- Safety and Effectiveness (BVS vs. XIENCE)
- Up to 2 *de novo* target lesions in separate coronary vessels

Trial Design

- Prospective, randomized 2:1, single-blind, multi-center

Primary Endpoint

- Target lesion failure (TLF) at 1 year

Powered Secondary Endpoints

- Angina at 1 year
- All revascularizations at 1 year
- Ischemia-driven target vessel revascularization (ID-TVR) at 1 year

Additional Secondary Endpoints

- Death (cardiac, vascular, non-vascular)
- Scaffold/stent thrombosis (per ARC definition):
  - Timing (acute, sub-acute, late, and very late)
  - Evidence (definite and probable)
- Composite Endpoints
  - Death/All MI
  - Cardiac Death/All MI
  - Cardiac Death/TV-MI/ID-TLR (TLF)
  - Cardiac Death/All MI/ID-TLR (MACE)
  - Cardiac Death/All MI/ID-TLR/ID-TVR, non TL (TVF)
  - Death/All MI/All revascularization

Key Clinical Inclusion Criteria

- Evidence of myocardial ischemia
- One or two *de novo* lesions, each in a different native coronary vessel
- RVD ≥2.5 mm and ≤3.75 mm
- Target Lesions ≤24 mm in length
- Diameter Stenosis ≥50% and <100% with a TIMI flow of ≥1

Vessel and lesion measurements by visual estimation with adjunctive imaging optional (QCA, IVUS, or OCT)

Key Exclusion Criteria

- **Patient Characteristics**
  - Recent MI (within 72 hours of MI and both CK and CK-MB have not returned to within normal limits at the time of index procedure)
  - Significantly reduced LV function (EF< 30%)
  - Renal insufficiency (GFR <30 ml/min/1.73m2 or on dialysis)
  - Requiring long-term anticoagulation.
- **Target Lesion/Vessel Characteristics**
  - Heavily calcified or tortuous vessels
  - Within or distal to a diseased coronary bypass graft
  - Left Main Lesion
  - Ostial and Aorto-ostial lesions (within 3 mm of vessel origin)
  - Vessel contains thrombus
  - Bifurcations Lesions with a

Side branch ≥ 2 mm in diameter, or
Side branch with either an ostial or non-ostial lesion with diameter stenosis > 50%, or
Side branch requiring dilatation

PCI Treatment

Pre- and Post-dilation

- **Successful Pre-dilation mandatory**
  - Residual %DS <40%
  - TIMI-3 flow
  - Lesion length (including any edge dissection) ≤24 mm
  - No other significant angiographic or clinical complications

- **Post dilation optional**
  - noncompliant balloon
  - Do not dilate to >0.5 mm beyond the nominal BVS diameter (due to concern of strut fracture)

Selected Demographics & Clinical Characteristics

	Absorb (N=1322)	XIENCE (N=686)	Difference [95% CI]
Characteristic			
Age (year)	63.5 ± 10.6 (1322)	63.6 ± 10.3 (686)	-0.2 [-1.1, 0.8]
Male Subjects	70.7% (934/1322)	70.1% (481/686)	0.53% [-3.62%, 4.80%]
Current Tobacco Use	21.3% (281/1322)	20.7% (142/686)	0.56% [-3.28%, 4.22%]
Any Diabetes Mellitus (DM)	31.5% (416/1320)	32.7% (224/686)	-1.14% [-5.49%, 3.12%]
Hypertension req. Med.	81.0% (1071/1322)	80.6% (553/686)	0.40% [-3.15%, 4.12%]
Dyslipidemia req. Med.	76.3% (1009/1322)	77.7% (533/686)	-1.37% [-5.16%, 2.57%]
Prior MI	21.5% (282/1311)	22.0% (150/681)	-0.52% [-4.42%, 3.23%]
Clinical Presentation			
Stable Angina	57.3% (757/1321)	60.8% (417/686)	-3.48% [-7.96%, 1.07%]
Single diseased artery	69.5% (919/1322)	67.2% (461/686)	2.31% [-1.93%, 6.65%]

Baseline Lesion Characteristics and QCA

by Angiographic Core Lab
Per-Subject Analysis (Primary Analysis Group, ITT Population)

	Absorb (N=1322) (L=1385)	XIENCE (N=686) (L=713)	Difference [95% CI]
Lesion Morphology			
Type B2/C	68.7% (949/1381)	72.5% (513/708)	-3.74% [-7.77%, 0.42%]
Calcification (moderate/severe)	33.1% (457/1379)	32.1% (227/708)	1.08% [-3.21%, 5.26%]
Bifurcations	37.0% (510/1380)	37.4% (264/706)	-0.44% [-4.85%, 3.90%]
Tortuosity (moderate/severe)	2.9% (40/1380)	4.0% (28/708)	-1.06% [-2.92%, 0.52%]

Procedural QCA Results by Angiographic Core Lab

Per-Subject Analysis (Primary Analysis Group, ITT Population)

	Absorb BVS (N=1322) (L=1385)	XIENCE (N=686) (L=713)	Difference [95% CI]
Pre-Procedure Measurement by QCA			
Lesion Length (mm)	12.60 ± 5.41 (1378)	13.12 ± 5.82 (708)	-0.52 [-1.04, -0.01]
RVD (mm)	2.67 ± 0.45 (1380)	2.65 ± 0.46 (708)	0.02 [-0.02, 0.06]
MLD (mm)	0.92 ± 0.37 (1380)	0.90 ± 0.34 (708)	0.03 [-0.01, 0.06]
%DS	65.25 ± 12.48 (1380)	65.90 ± 11.66 (708)	-0.65 [-1.74, 0.43]
Post Pre-Dilatation Measurement by QCA			
MLD (mm)	1.56 ± 0.45 (1303)	1.51 ± 0.43 (648)	0.04 [0.00, 0.09]
%DS	41.41 ± 14.55 (1303)	42.84 ± 14.02 (648)	-1.43 [-2.77, -0.09]

Procedural Results by Angiographic Core Lab

(Primary Analysis Group, ITT Population)

	Absorb BVS (N=1322) (L=1385)	XIENCE (N=686) (L=713)	Difference [95% CI]
Number of Lesions treated (Per Subject Analysis)			
One Lesion Treated (%)	84.0 (1110/1322)	82.7 (567/686)	1.31[-2.06%, 4.86%]
Post-Procedure Measurement by QCA (Per-Lesion Analysis)			
RVD (mm)	2.70 ± 0.45 (1374)	2.68 ± 0.47 (706)	0.02 [-0.02, 0.06]
In-Segment			
MLD (mm)	2.15 ± 0.41 (1374)	2.14 ± 0.43 (706)	0.01 [-0.03, 0.05]
%DS	20.04 ± 7.94 (1374)	19.82 ± 8.20 (706)	0.23 [-0.51, 0.96]
Acute Gain (mm)	1.23 ± 0.46 (1373)	1.24 ± 0.44 (706)	-0.01 [-0.05, 0.03]
In-Device			
MLD (mm)	2.37 ± 0.40 (1373)	2.49 ± 0.40 (706)	-0.12 [-0.15, -0.08]
Acute Gain (mm)	1.45 ± 0.45 (1372)	1.59 ± 0.44 (706)	-0.14 [-0.18, -0.10]
%DS	11.62 ± 8.77 (1369)	6.41 ± 8.91 (702)	5.21 [4.40, 6.02]
Total Stent/Scaffold Length (mm)	18.02 ± 6.43 (1373)	19.13 ± 7.62 (706)	-1.11 [-1.77, -0.45]

Procedural QCA Results by Angiographic Core Lab

Per lesion Analysis (Primary Analysis Group, ITT Population)

	BVS	XIENCE
% with Post Dilatation	64.8%	49.9%
Maximum Post- dil. Balloon Pressure (Median)	16 atm	16 atm
Ratio: Balloon* Diameter/Post Procedure RVD (Median) *post dilatation balloon	1.2	1.18

Antiplatelet Medication Usage for the Index Procedure

Per-Subject Analysis, Intent-to-Treat Population

	Absorb (N=1322)	XIENCE (N=686)	p-value
Aspirin	99.3% (1313/1322)	99.3% (681/686)	1.0
P2Y12 Receptor Antagonist	99.0% (1309/1322)	98.8% (678/686)	0.70
Clopidogrel	62.6% (827/1322)	64.7% (444/686)	0.34
Prasugrel or Ticagrelor	36.5% (483/1322)	34.4% (236/686)	0.34

Antiplatelet Agent Use at 30 Days and 1 Year

Per-Subject Analysis, Intent-to-Treat Population

	Absorb (N=1322) %	XIENCE (N=686) %	p-value
Use at 30 days			
Aspirin	98.6 (1303/1322)	99.0 (679/686)	0.43
P2Y12 receptor inhibitor	99.0 (1309/1322)	99.1(680/686)	0.81
Clopidogrel	68.3 (903/1322)	72.0 (494/686)	0.09
Prasugrel or ticagrelor	32.4 (428/1322)	28.1(193/686)	0.05
Use at 1 year			
Aspirin	95.8 (1267/1322)	95.8 (657/686)	0.94
P2Y12 receptor inhibitor	94.4 (1248/1322)	95.0 (652/686)	0.55
Clopidogrel	67.5 (893/1322)	72.2 (495/686)	0.03
Prasugrel or ticagrelor	26.9 (355/1322)	22.9 (157/686)	0.05

Pre-Specified Analysis Populations

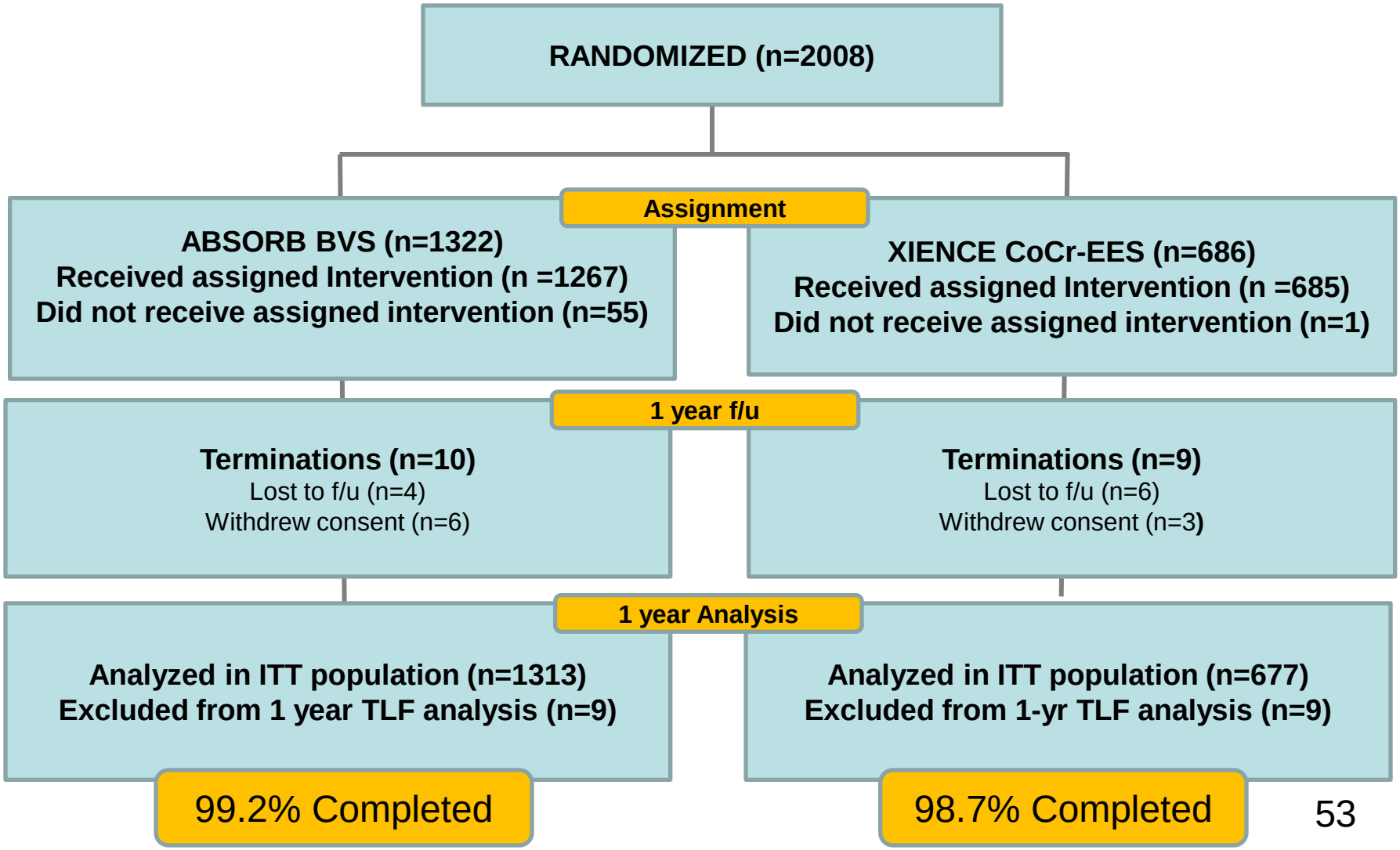
Intent-To-Treat (ITT) Population

- Primary Analysis Population
- Subjects are analyzed in the treatment group to which they were randomized.

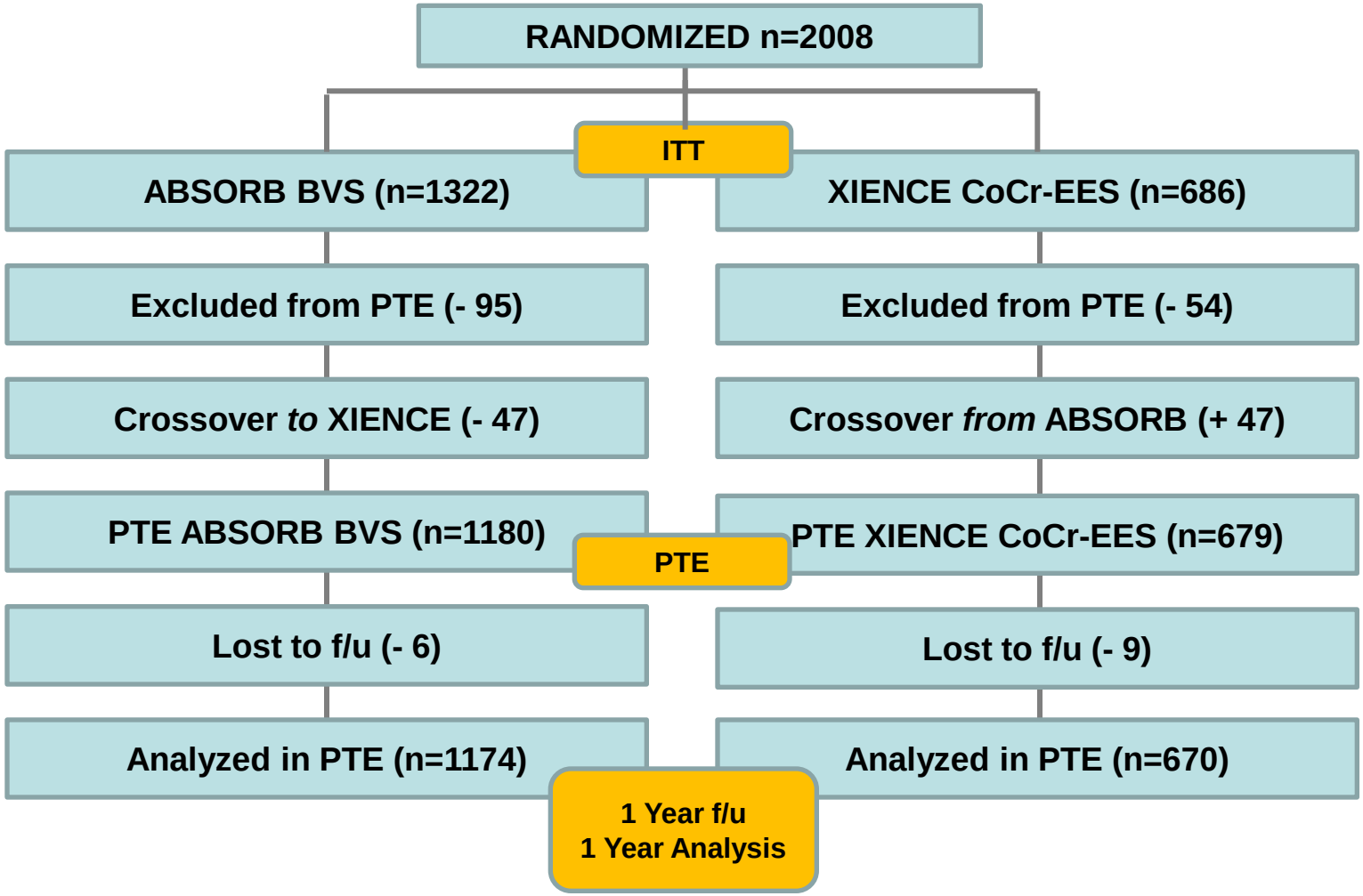
Per-Treatment-Evaluable (PTE) Population

- Received only study device(s) at the target lesion.
- Analyzed based on the treatment actually received (includes crossovers)
- Excludes subjects with major protocol deviations

Patient Flow for the ITT Population



Patient Flow for PTE Population



FDA Presentations

- Introduction and Regulatory History
  - Dr. Kenya Brothers
- Statistical Presentation
  - Dr. Yu Zhao
- Clinical Presentation – Overview
  - Dr. Adrian Magee
- Clinical Presentation – Clinical Results
  - Dr. Andrew Farb
- Post-Approval Considerations
  - Dr. Nadezda Radoja
- Summary
  - Dr. Kenya Brothers

ABSORB BVS Clinical Results

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Division of Cardiovascular Devices
Center for Devices and Radiological Health

Center for Devices and Radiological Health
CDRH

Outline

- ABSORB III in depth
  - Acute device and clinical procedure success rates
  - Target lesion failure primary endpoint
    - Analysis populations: ITT, As-Treated, and Per Treatment Evaluable (PTE)
  - Considering the BVS within a risk-benefit framework

Risk/Safety	Benefit/Effectiveness
• ITT population • Small vessels • Approaches to mitigating risk o Appropriate target vessel selection and BVS post-dilatation	• TLR • Major secondary endpoints

- Supplementary non-US BVS studies
- Concluding remarks

ABSORB III Acute Device and Procedural Success Definitions

- Device success (lesion-based)
  - Successful delivery and deployment of the study scaffold/stent at the intended target lesion
  - Successful withdrawal of the delivery system
  - Residual stenosis <30%
- Clinical procedure success (patient-based)
  - Device success at target lesion(s)
  - No occurrence of cardiac death, target vessel MI, or repeat TLR during the hospital stay (maximum of 7 days)

Acute Device and Clinical Procedural Success

	BVS N=1322, L=1385	XIENCE N=686, L=713	Difference [95% CI]
Device Success	94.3% (1278/1355)	99.3% (699/704)	-4.97% [-6.39%, -3.52%]
Clinical Procedure Success	94.6% (1240/1311)	96.2% (652/678)	-1.58% [-3.40%, 0.46%]

N=Subjects, L=Lesions

Lower rate of device success in the BVS group

Use of Unassigned Devices

	BVS	XIENCE
Total	71	6
Failure to deliver/cross	40	2
Implanted assigned device plus other device due to bailout	10	0
BVS inventory lacking	12	NA
Randomization error or physician decision	4	2
Other*	4	1
Unknown	1	1

2:1 randomization BVS:XIENCE

BVS Target Lesion Delivery/Cross Failures

		Deliverability Failure (N=40)
Diameter stenosis	<median of the BVS ITT population	13/40 (32.5%)
	≥median of the BVS ITT population	27/40 (67.5%)
Lesion length	<median of the BVS ITT population	16/38 (42.1%)
	≥median of the BVS ITT population	22/38 (57.9%)
Angulation	<median of the BVS ITT population	10/39 (25.6%)
	≥median of the BVS ITT population	29/39 (74.4%)
Calcification	None/mild	18/40 (45.0%)
	Moderate/severe	22/40 (55.0%)

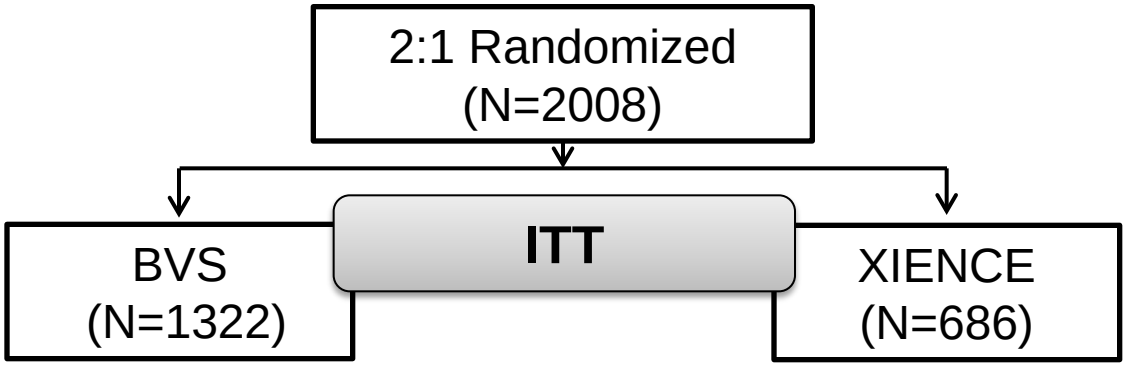
Only 40 subjects with failure to deliver/cross out of a total of 1322 BVS ITT subjects (3.0%)

1-Year TLF Primary Endpoint

ITT vs. As-Treated vs. PTE Populations

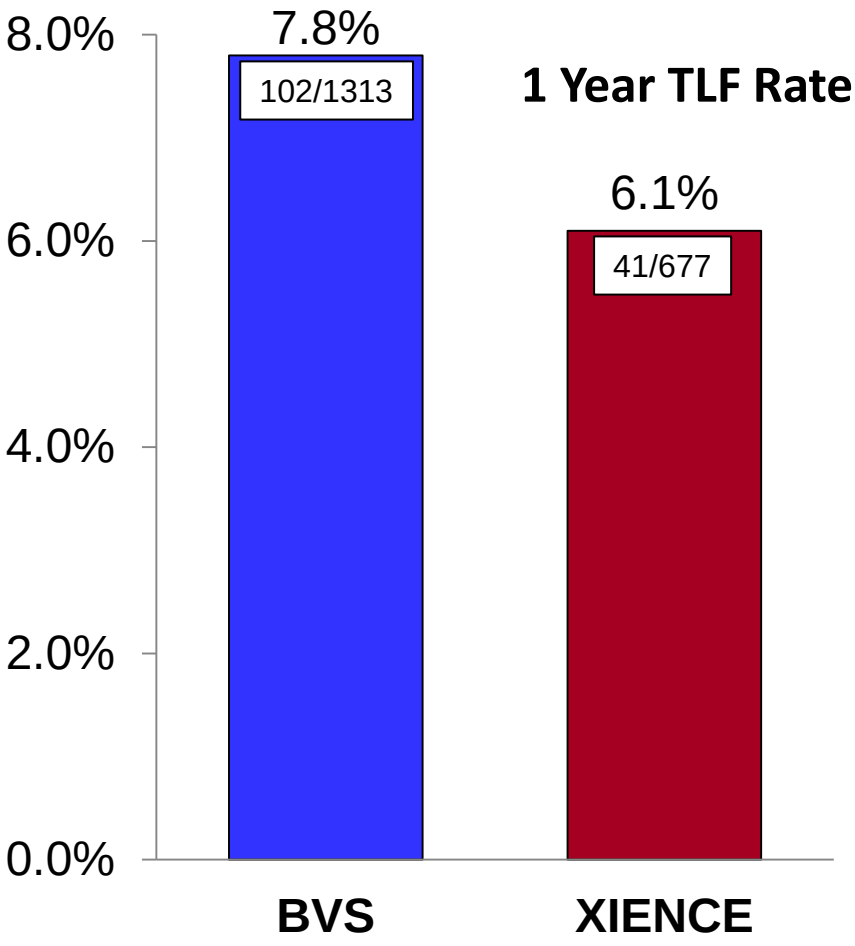
Is the BVS clinically non-inferior to Xience?

Analysis Populations

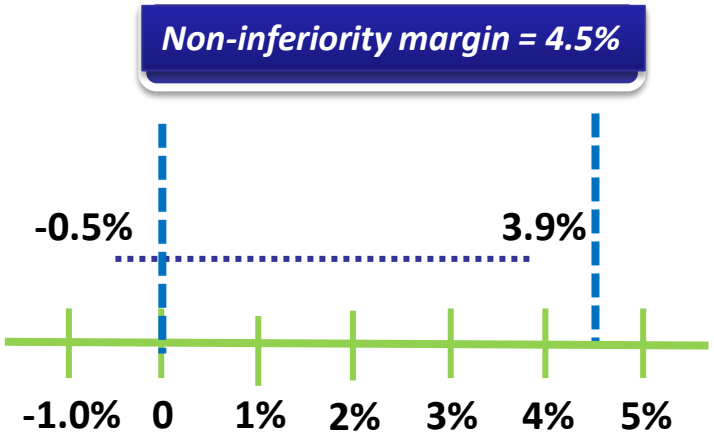


1-Year TLF Primary Endpoint

ITT Population



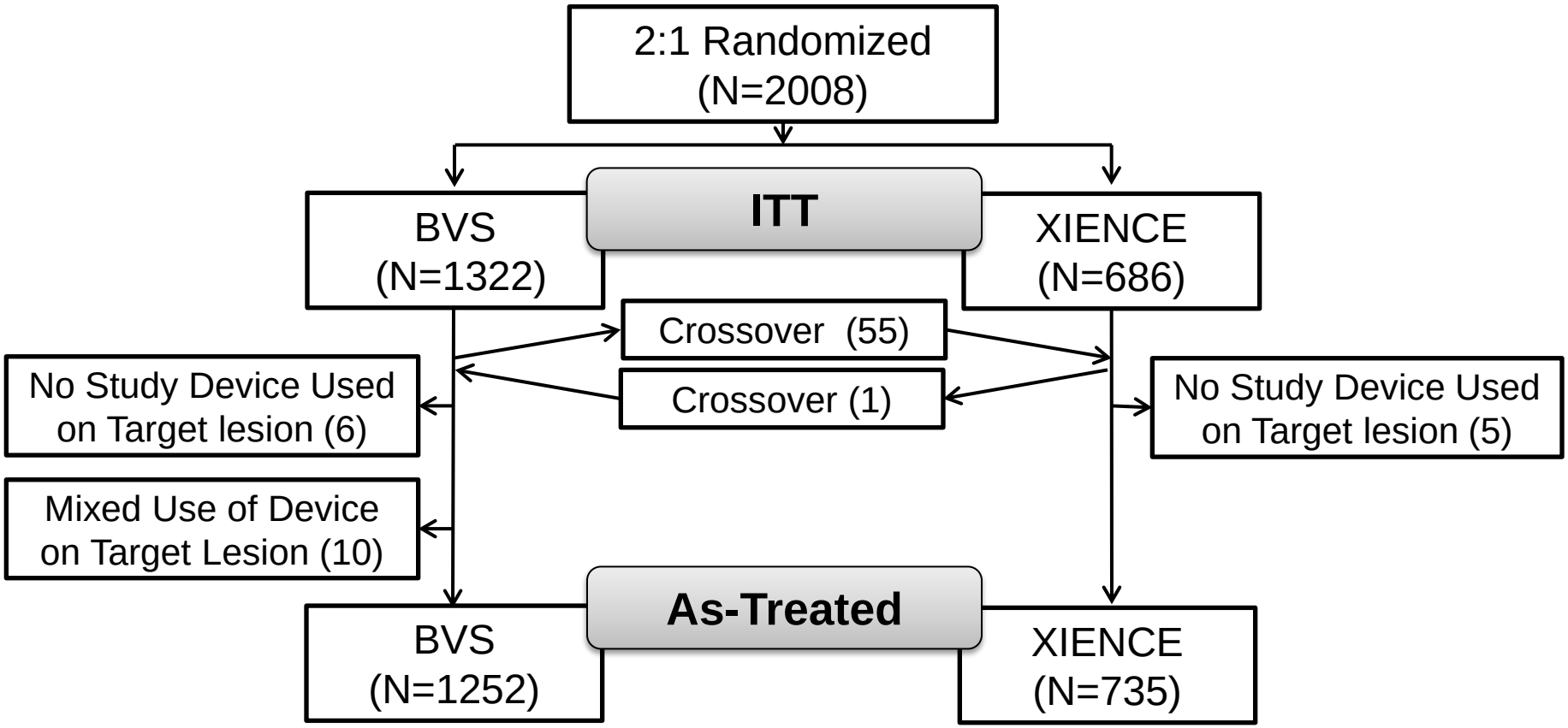
1 Year TLF Rate Difference = 1.7%



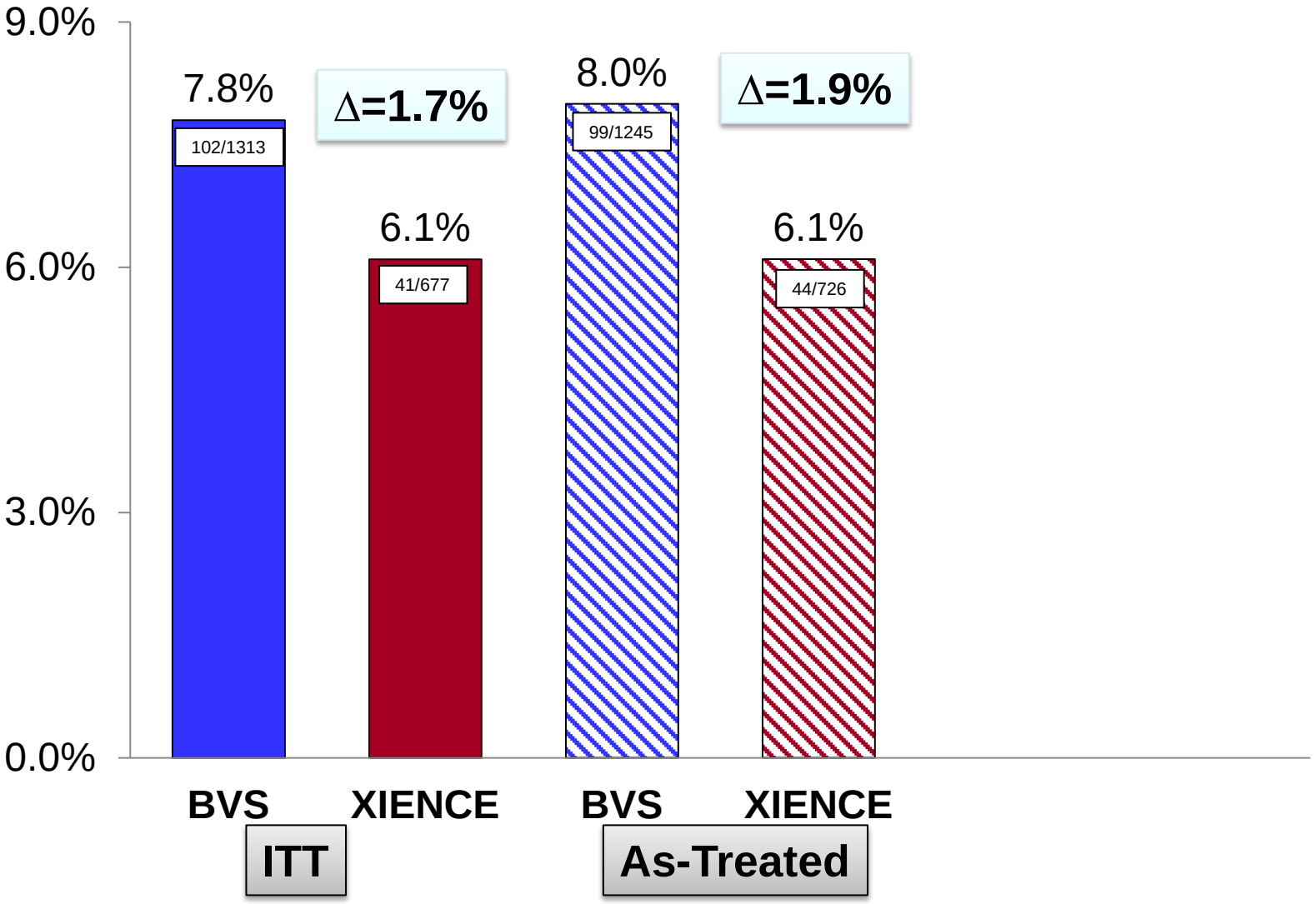
$P_{non\text{-}inferiority} = 0.007$

Non-inferiority met

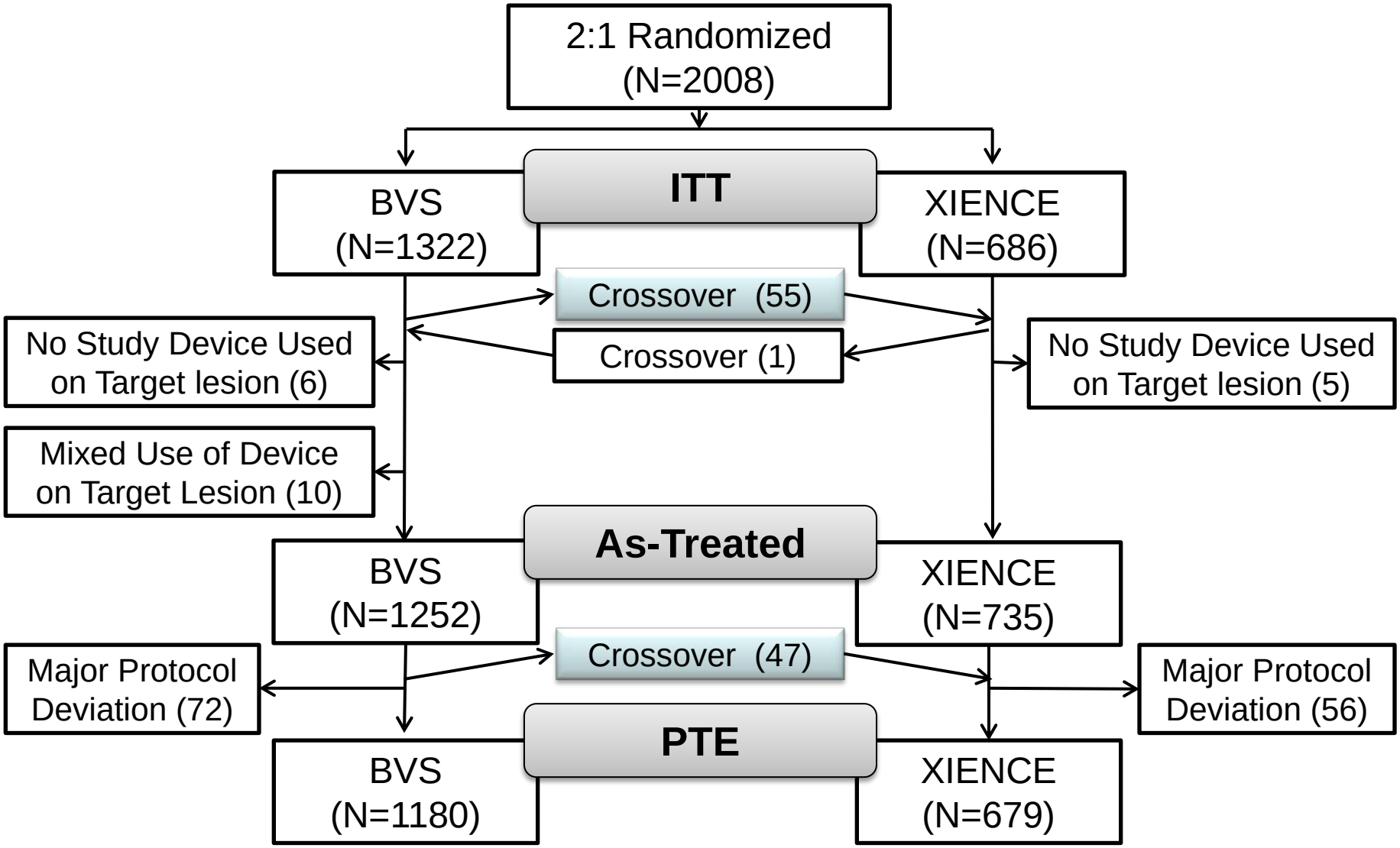
Analysis Populations



1-Year TLF Primary Endpoint
ITT vs. As-Treated

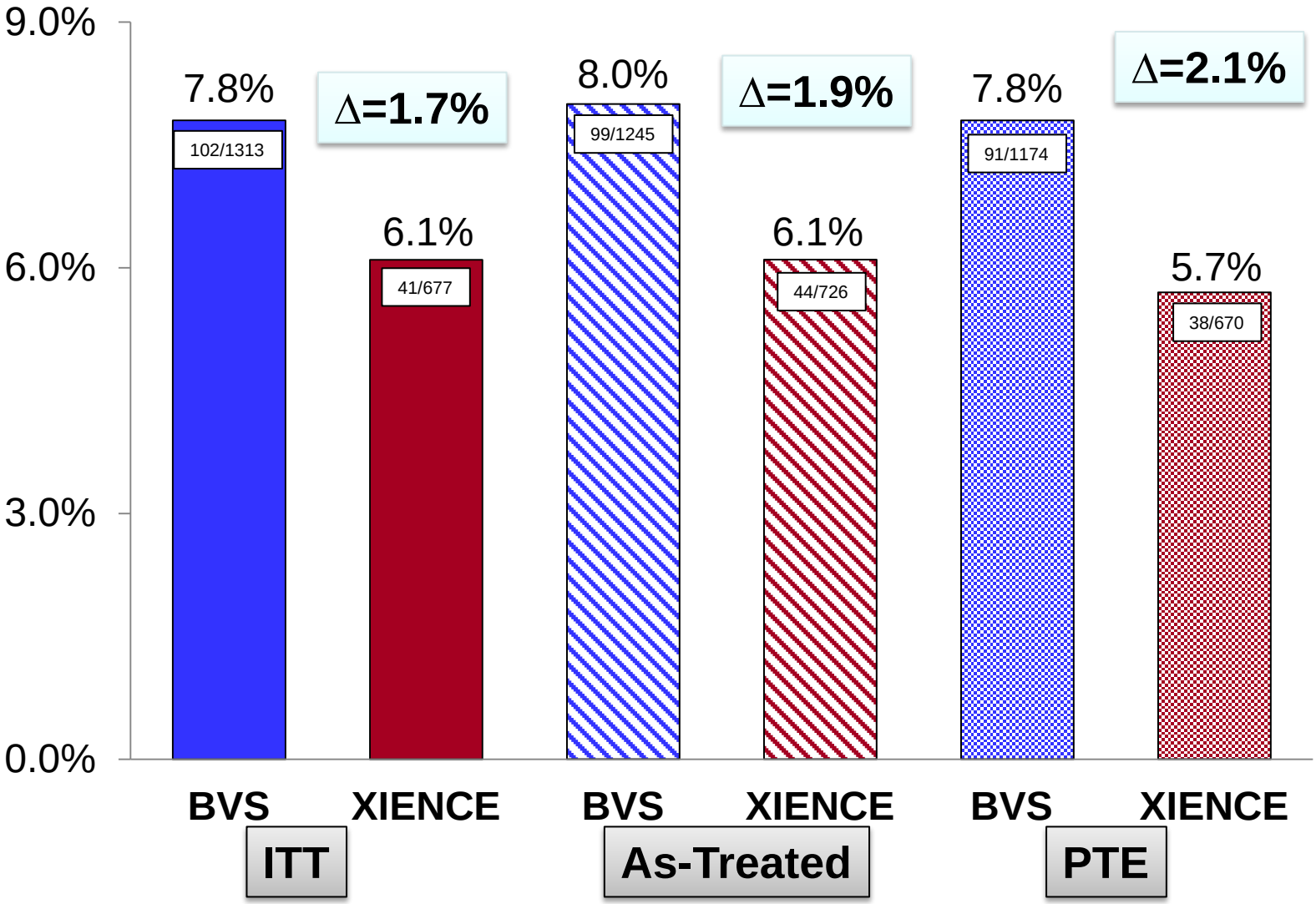


Analysis Populations



1-Year TLF Primary Endpoint

ITT vs. As-Treated vs. PTE



FDA Perspectives on BVS Non-Inferiority

- At 1-year follow-up:
  - In the ITT population, the non-inferiority objective was met
    - The observed 1-year TLF rate difference was 1.7% in favor of the XIENCE group (6.1%) vs. the BVS group (7.8%).
  - In the As-Treated and PTE populations, which were analyzed based on the treatment actually received (crossovers included in AT and PTE, and subjects with major protocol deviations excluded in PTE), there was a higher observed TLF rate difference favoring XIENCE.

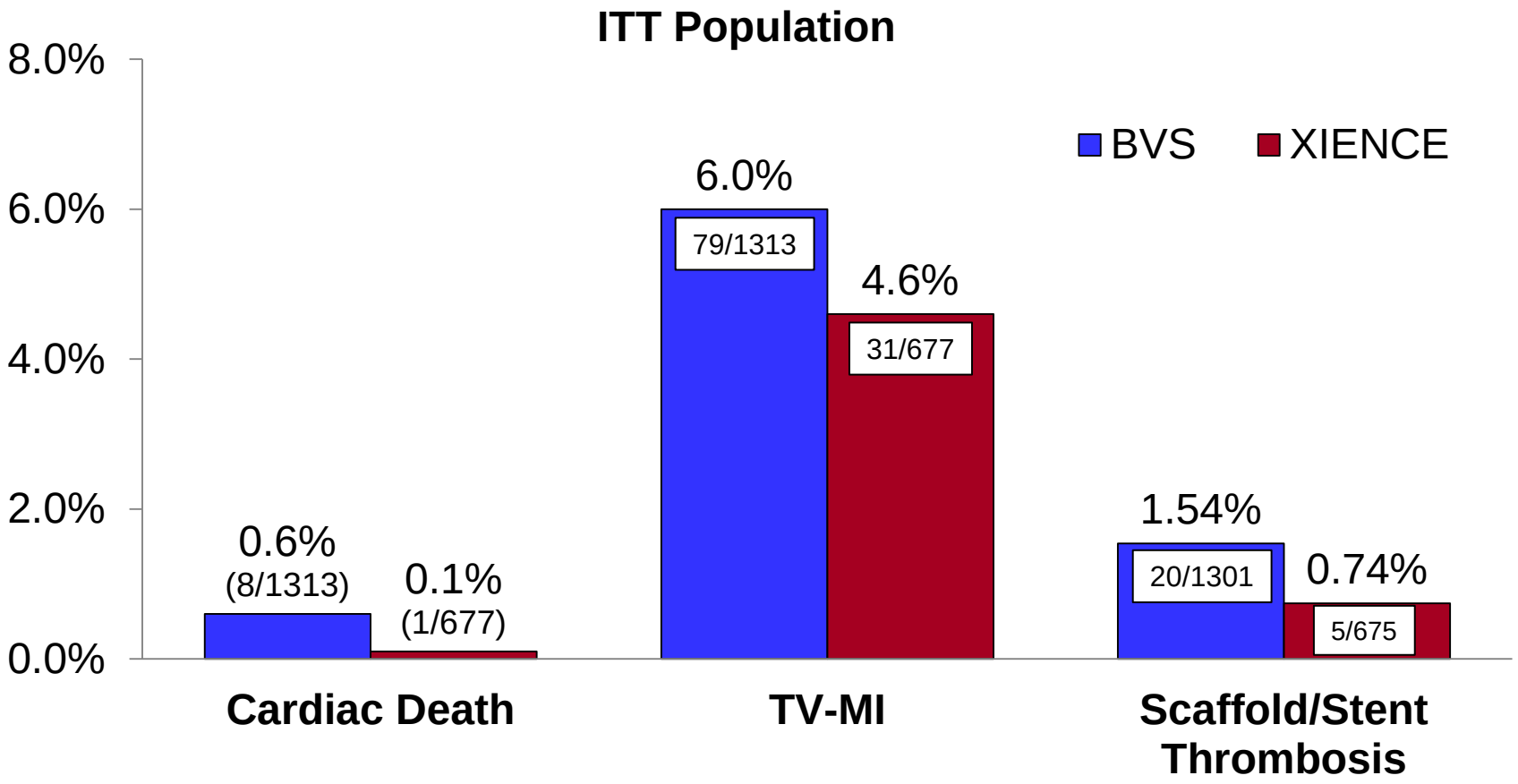
Population	1-Year TLF Rate Difference (BVS – XIENCE)
ITT	1.7%
As-Treated	1.9%
PTE	2.1%

Considering the BVS Within a Risk-Benefit Framework

Risks/Safety

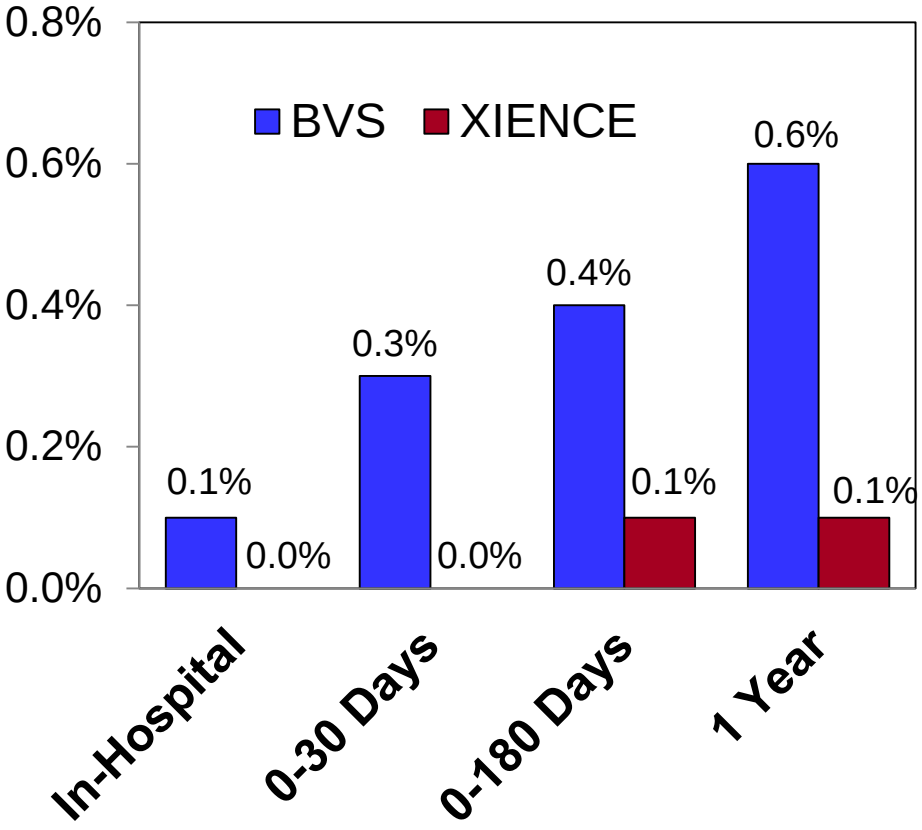
Safety Events at 1-Year

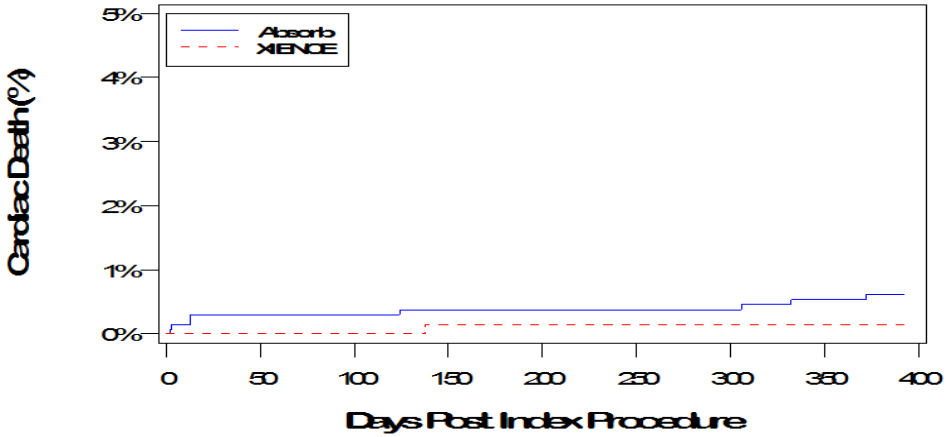
Cardiac Death, TV-MI, and Scaffold/Stent Thrombosis



Cardiac Death at 1-Year

ITT Population

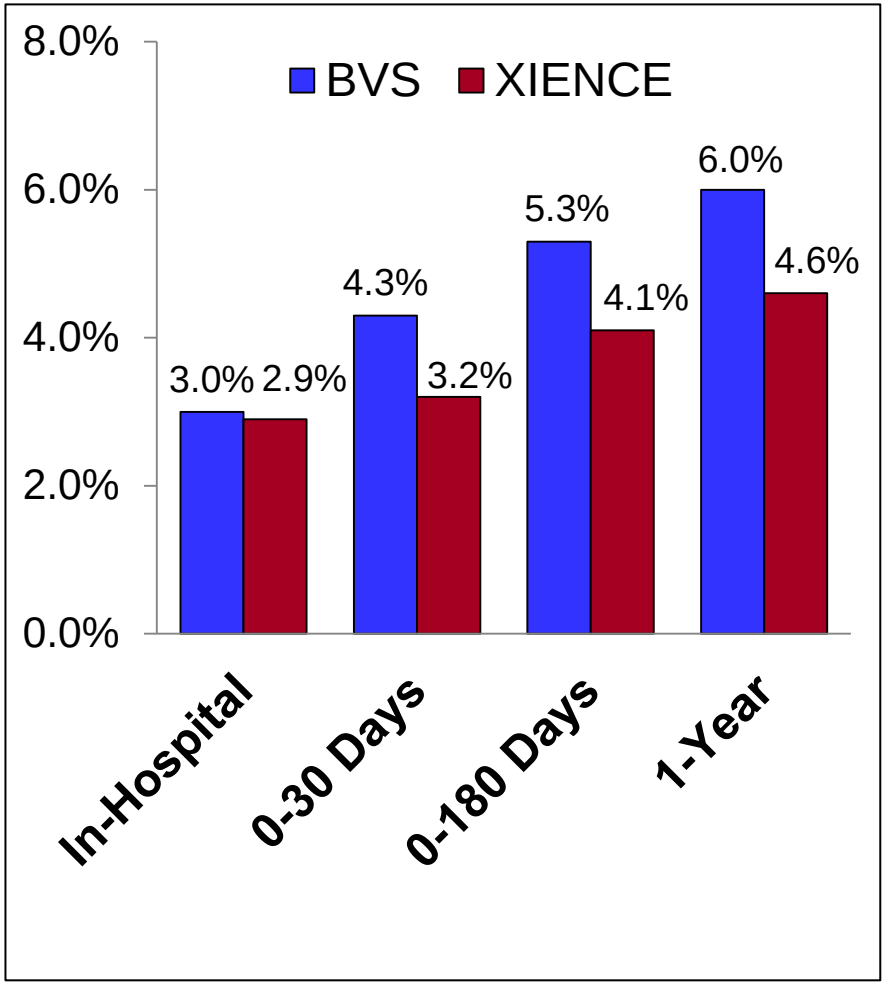


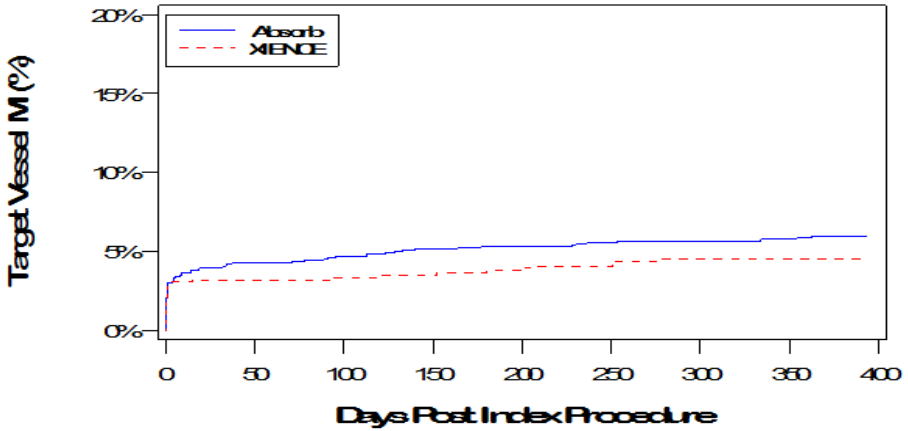


- **Low rates of cardiac death in both groups (<1%)**
- **1 Year rate difference (BVS - XIENCE) = 0.46%**

Target Vessel MI at 1-Year

ITT Population

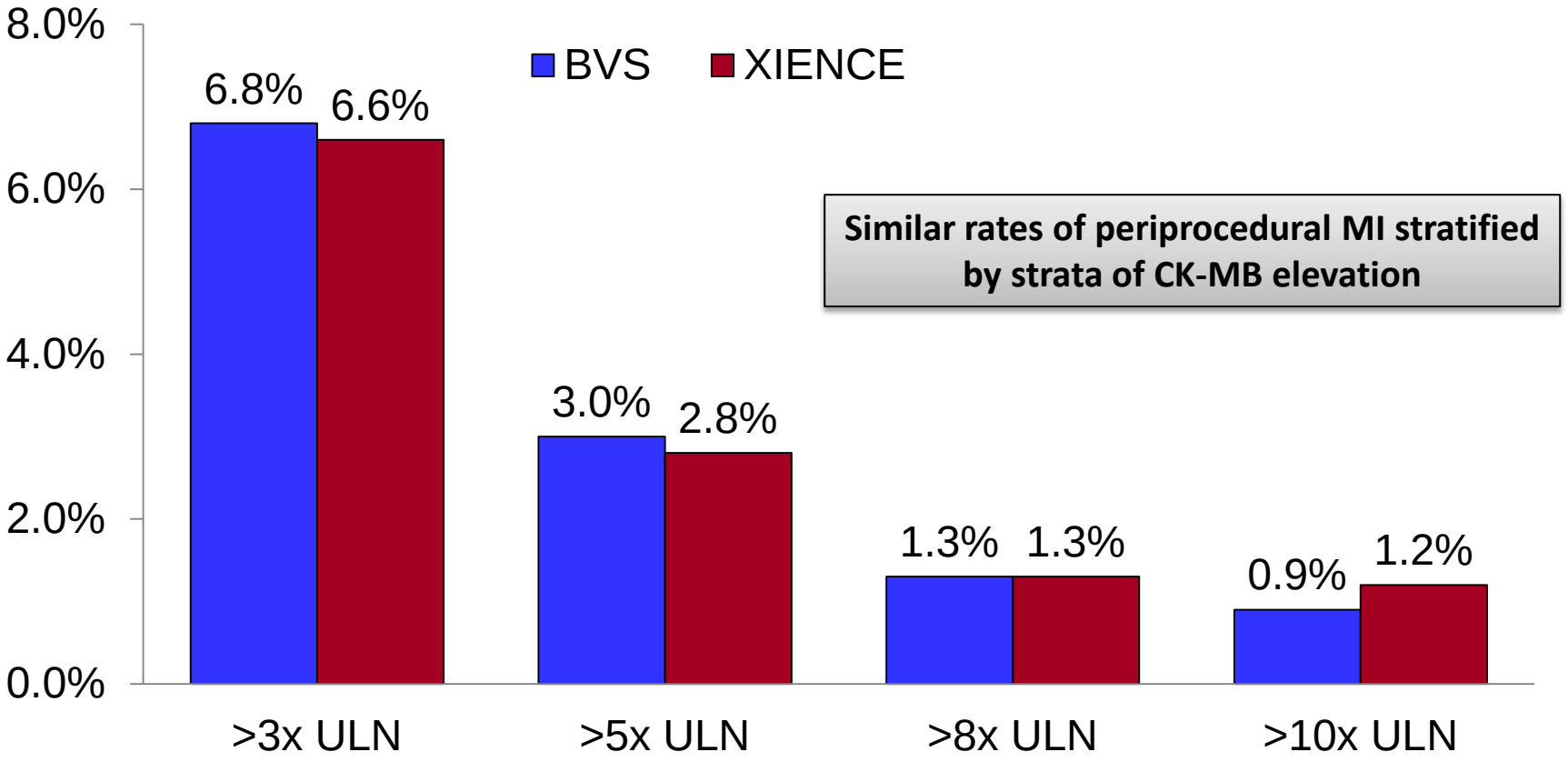




- Slightly increasing TV-MI rate difference over the course of 1 year favoring XIENCE
- 1 Year rate difference (BVS - XIENCE) = 1.44%

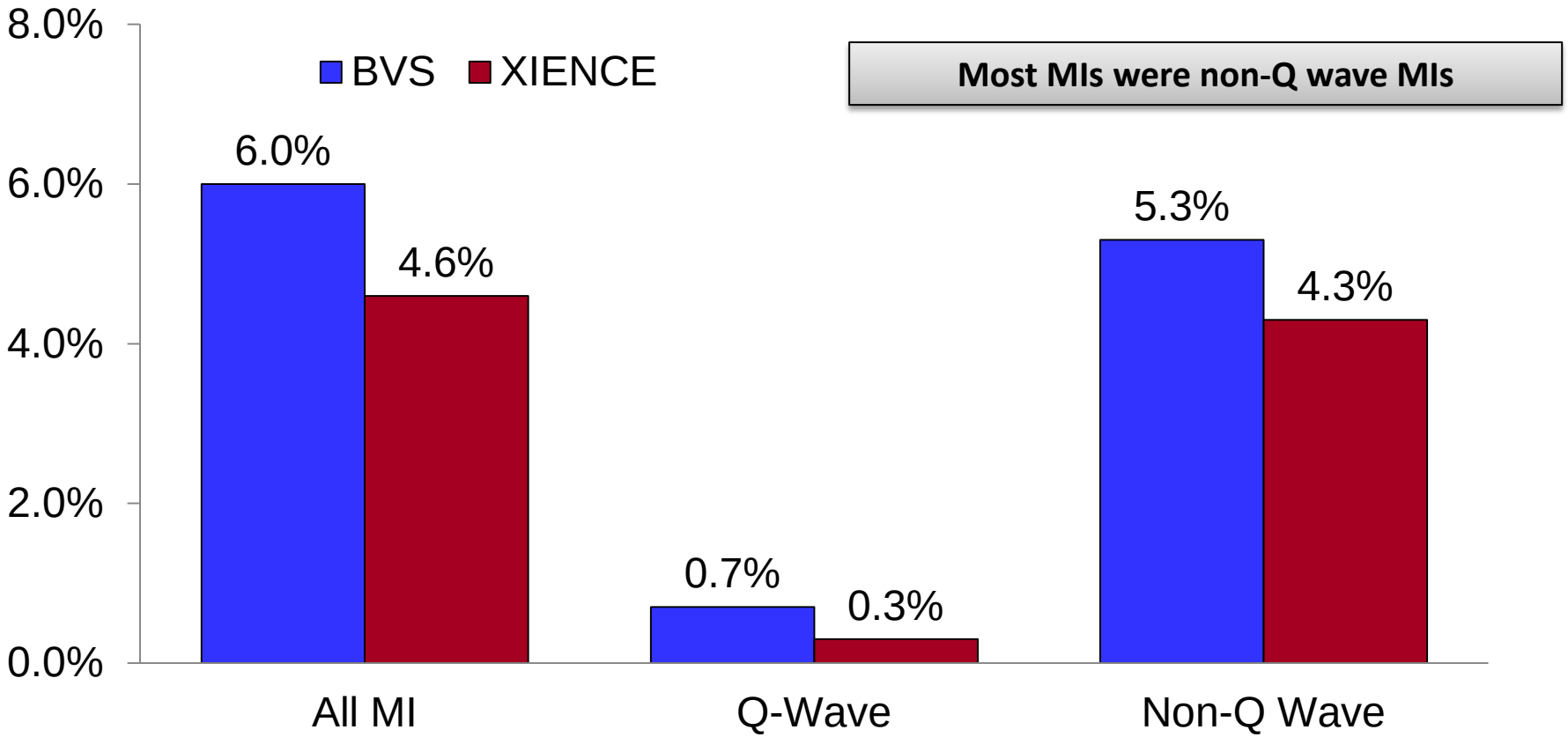
Periprocedural Target Vessel MI

ITT Population



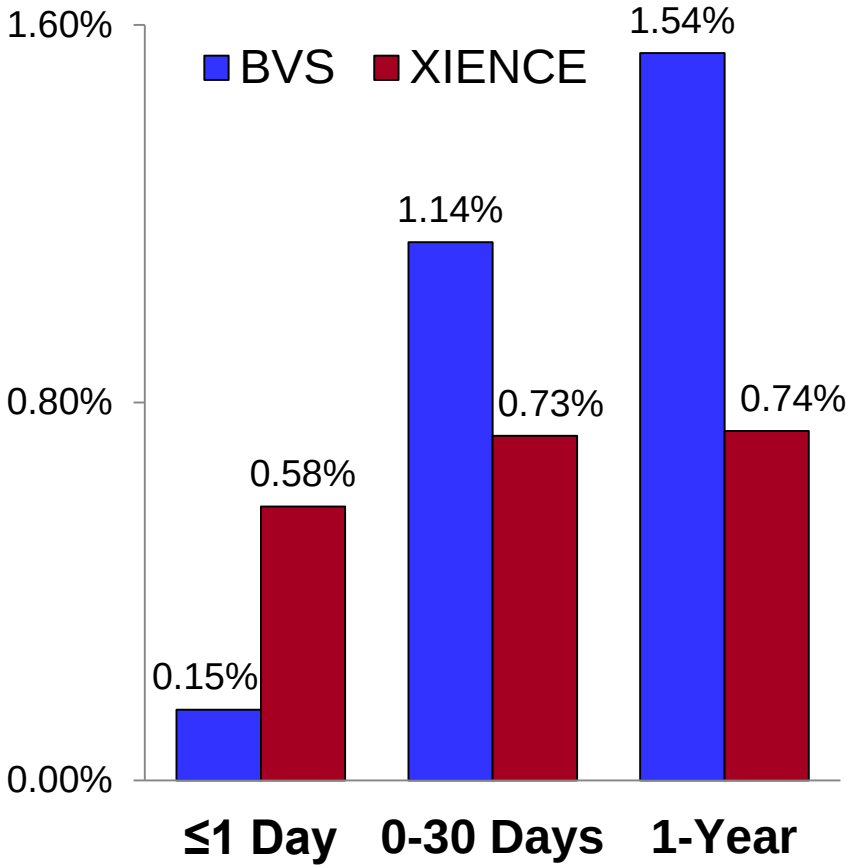
Target Vessel MI at 1-Year

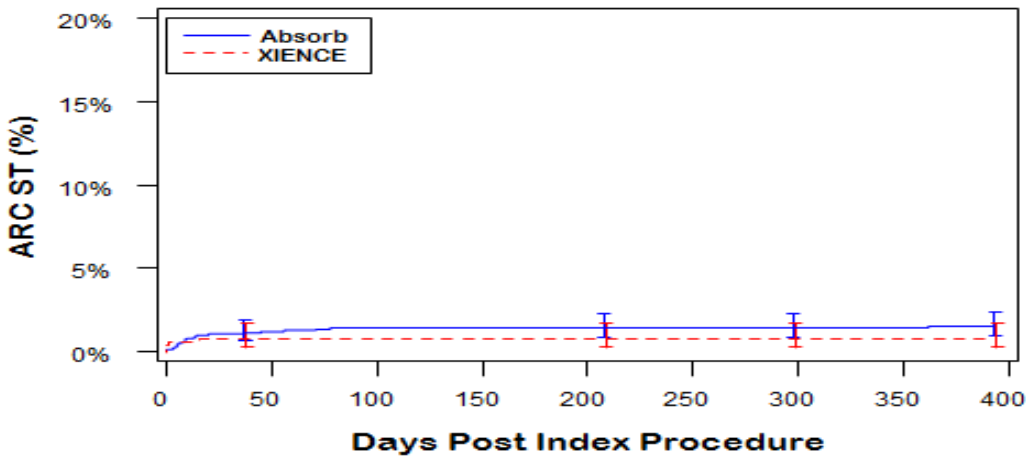
ITT Population



Scaffold/Stent Thrombosis at 1-Year

ITT Population





- **No XIENCE stent thrombosis cases after 30 days**
- **Increasing device thrombosis rate difference over the course of 1 year favoring XIENCE**
- **1 Year rate difference (BVS - XIENCE) = 0.80%, but >2-fold higher in the BVS group**
- **1 subject randomized to BVS treated with a XIENCE stent after unsuccessful BVS deployment**

Clinical Events Associated With Scaffold/Stent Thrombosis

	Implanted BVS (n=19) (Definite ST=17, Probable ST=2)	Implanted XIENCE (n=6) (Definite ST=6, Probable ST=0)
Death	2/19	0/6
TV-MI	14/19	5/6
TV QMI	8/19	1/6
TV NQMI	6/19	4/6
Unstable Angina	4/19	6/6
ID-TLR	17/19	6/6

2:1 randomization BVS:XIENCE. Subjects could be counted for more than one event. One subject with crossover from BVS to XIENCE counted in the XIENCE column.

- **The 2 BVS group deaths were sudden deaths within 30 days of the index procedure.**
- **14 of 19 BVS thrombosis cases and 5 of 6 Xience thrombosis cases were associated with acute MIs.**
- **17 of 19 subjects with BVS thrombosis cases and all 6 subjects with Xience thrombosis underwent TLR.**

Scaffold/Stent Thrombosis and Dual Antiplatelet Therapy (DAPT) Use

ITT Population	Scaffold/Stent Thrombosis at 1-Year	
	BVS	XIENCE
Total (N)	20	5
On ASA alone	3/20 (15%)	0/5 (0%)
On P_2Y_{12} inhibitor alone	0/20 (0%)	0/5 (0%)
On DAPT	16/20 (80%)	5/5 (100%)

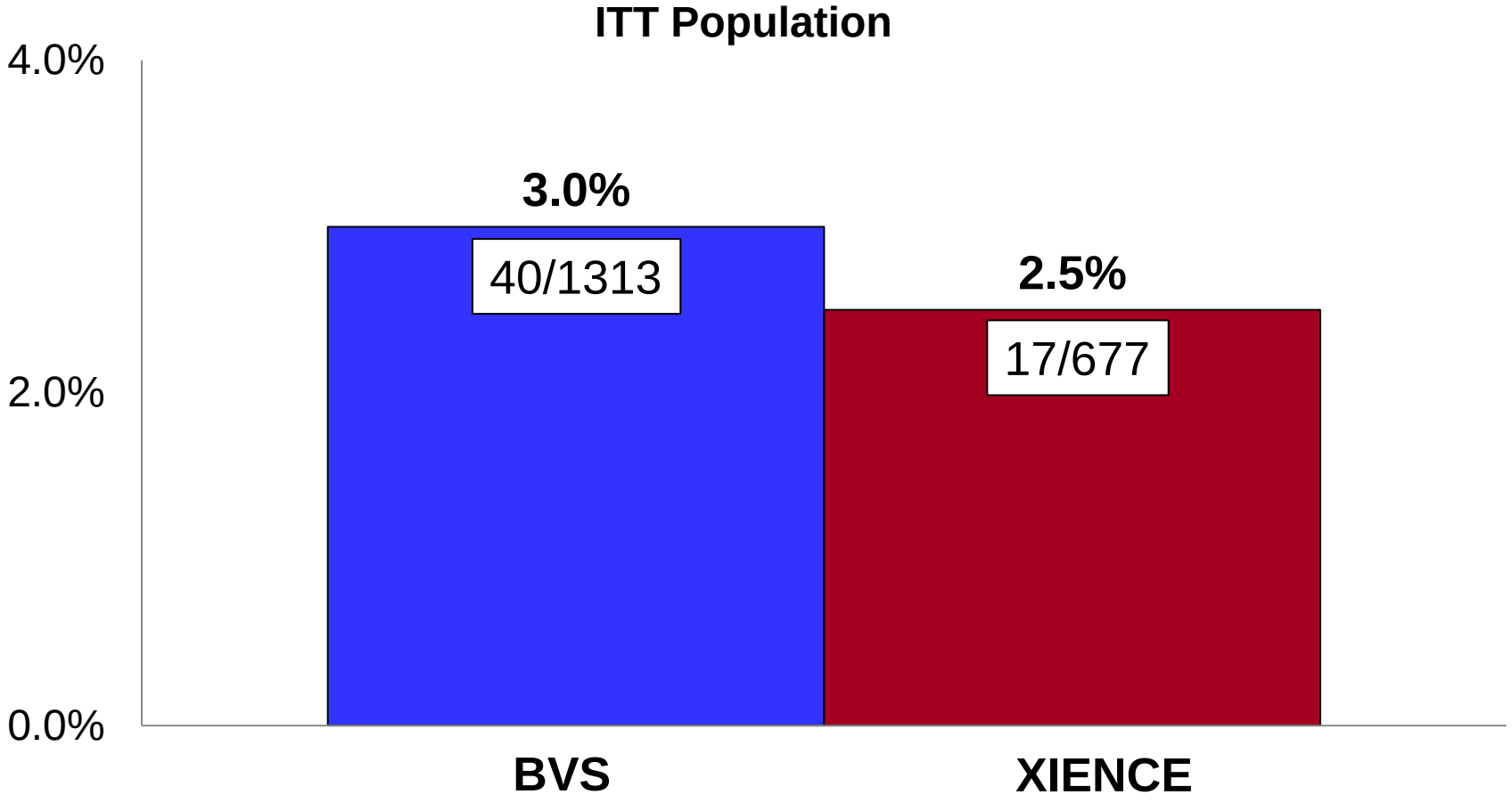
ARC Definite+Probable Stent Thrombosis Rates in Contemporary Major DES RCTs Reviewed by FDA

DES (Study)	Stent Thrombosis at 1-Year
Synergy (EVOLVE II RCT)	0.4% (3/832)
Promus Element (EVOLVE II RCT)	0.6% (5/808)
Promus Element (PLATINUM Workhorse)	0.4% (3/735)
Promus (PLATINUM Workhorse)	0.4% (3/725)
XIENCE (SPIRIT III)	0.9% (6/650)
XIENCE (SPIRIT IV)	0.29% (7/2391)
XIENCE (ABSORB III)	0.74% (5/675)
BVS (ABSORB III)	1.54% (20/1301)

Considering the BVS Within a Risk-Benefit Framework

Benefits/Effectiveness

Ischemia Drive Target Lesion Revascularization at 1-Year



Secondary Endpoints
Effectiveness Benefits

ITT population	BVS (N=1322)	XIENCE (N=686)	Difference (95% CI)*	P-Value
1-Year Angina	18.3% (238/1303)	18.4% (125/678)	-0.2% (-3.8%, 3.4%)	0.9256
1-Year All Revascularization	9.1% (120/1313)	8.1% (55/677)	1.0% (-1.6%, 3.6%)	NA
1-Year ID-TVR	5.0% (66/1313)	3.7% (25/677)	1.3% (-0.5%, 3.2%)	NA

*Without multiplicity adjustment

There was no signal of superiority of the BVS vs. XIENCE for the 1-year rates of angina, all revascularization, or ischemia-driven target vessel revascularization

Other Potential BVS Benefits

- Restoration on normal arterial vasomotion
- Late lumen enlargement
- Favorable plaque modification
- Avoidance of very late vascular responses to a metallic stent
- More options for future revascularization procedures (if needed)

The benefits to patients associated with these potential BVS benefits remain to be demonstrated in clinical studies

FDA Perspectives on BVS Safety (Risks) and Effectiveness (Benefits)

- At 1-year follow-up in ABSORB III:
  - The observed rates of the *safety components of the TLF endpoint* (cardiac death and target vessel MI) and scaffold/stent thrombosis were numerically higher in the BVS group.
    - The scaffold/stent thrombosis rate was >2-fold higher in the BVS group vs. the Xience group (1.54% vs. 0.74%).
  - The observed rate of the *effectiveness component of the TLF endpoint* (ischemia-driven TLR) was 3.0% in the BVS group and 2.5% in the XIENCE group.
  - There was no signal of superiority of the BVS vs. XIENCE for the 1-year rates of angina, all revascularization, or ID-TVR.

Considering the BVS Within a Risk-Benefit Framework

Risks/Safety

Can appropriately sized vessels be selected, and are there optimal deployment strategies established for the safe use of the BVS?

Clinical Outcomes in the Treatment of Small Target Vessels

Post-Hoc Analysis

ABSORB III Target Lesion Enrollment Criteria

- Native epicardial coronary artery location
- Visual estimation of target lesion dimensions from angiography:
  - Reference vessel diameter (RVD) following pre-dilatation ≥2.5 mm and ≤3.75 mm
  - Lesion length ≤24 mm
  - Diameter stenosis of ≥50% and <100%

Use of quantitative vessel sizing methods such as quantitative coronary angiography (QCA), IVUS, or OCT optional

Vessel vs. Quantitative Measurement of Coronary Artery Dimensions

- Visual estimates of coronary dimensions typically overestimate true vessel diameters measured by QCA.
  - Precise overestimation of vessel diameters by visual assessment is not known, 0.25 mm is a reasonable approximation (Popma, et al. Am J Cardiol 1997;80:19K–25K)
    - A 2.50 mm visually estimated diameter correlates with a 2.25 mm QCA-measured diameter.
    - A QCA-assessed RVD <2.25 mm could be interpreted as an undersized target vessel per the ABSORB III inclusion criterion of a visually estimated RVD ≥2.5 mm.

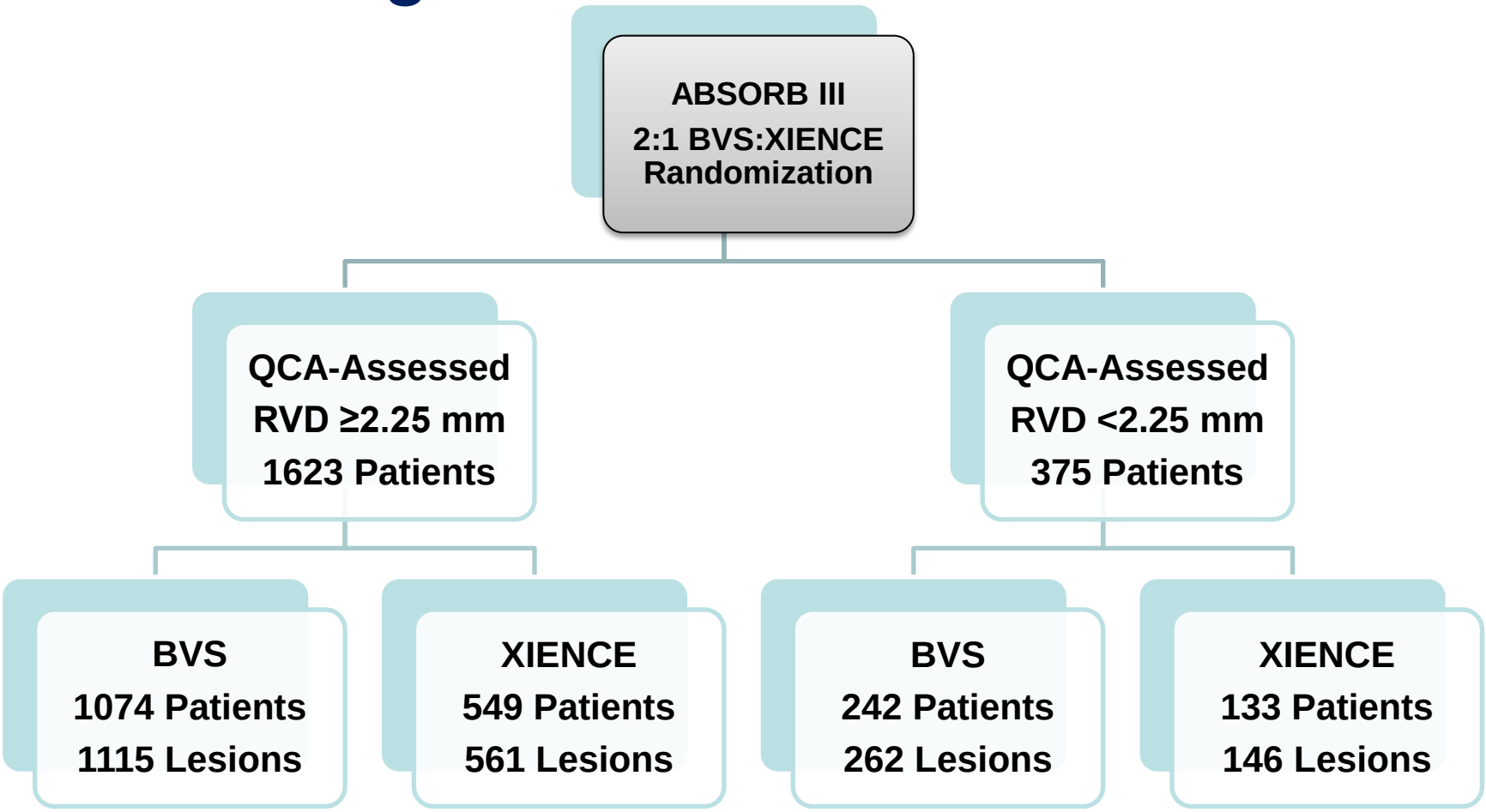
Frequency of Small Vessel Treatment in ABSORB III

QCA-Assessed RVD <2.25 mm

Angiographic core lab evaluation

ABSORB III	Total	BVS	XIENCE
Proportion of Subjects With Treatment of an <2.25 mm Artery	18.7% (375/1998)	18.4% (242/1316)	19.5% (133/682)

ABSORB III Post Hoc Target Vessel Stratification



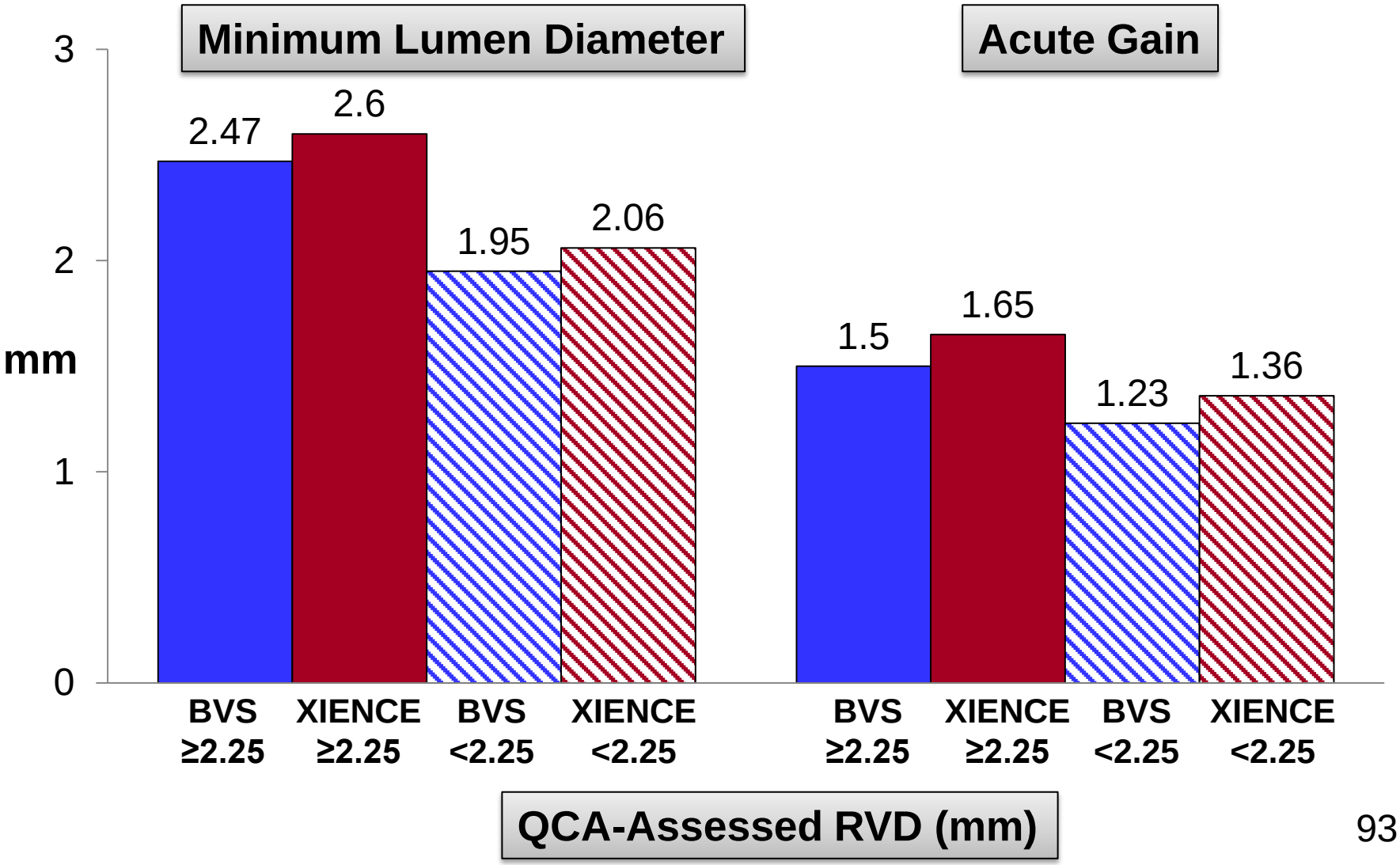
Clinical Features Stratified by Vessel Size

	RVD ≥2.25 mm		RVD <2.25 mm	
	BVS (N=1074)	XIENCE (N=549)	BVS (N=242)	XIENCE (N=133)
Age (year)	63.3 ± 10.6	63.3 ± 10.2	64.5 ± 10.9	64.9 ± 10.7
Male Subjects	71.5%	73.0%	66.5%	57.1%
Current Tobacco Use	20.9%	20.2%	22.3%	22.6%
Diabetes Mellitus	30.3%	32.2%	36.5%	33.8%
Hypertension requiring meds	80.5%	80.0%	83.5%	84.2%
Dyslipidemia requiring meds	75.9%	77.8%	78.1%	77.4%
Prior Coronary Intervention	37.4%	37.5%	45.0%	41.2%
Prior MI	21.1%	20.5%	23.4%	29.0%
Unstable Angina	27.1%	26.2%	25.6%	18.0%
Stable Angina	57.2%	59.9%	57.4%	63.9%

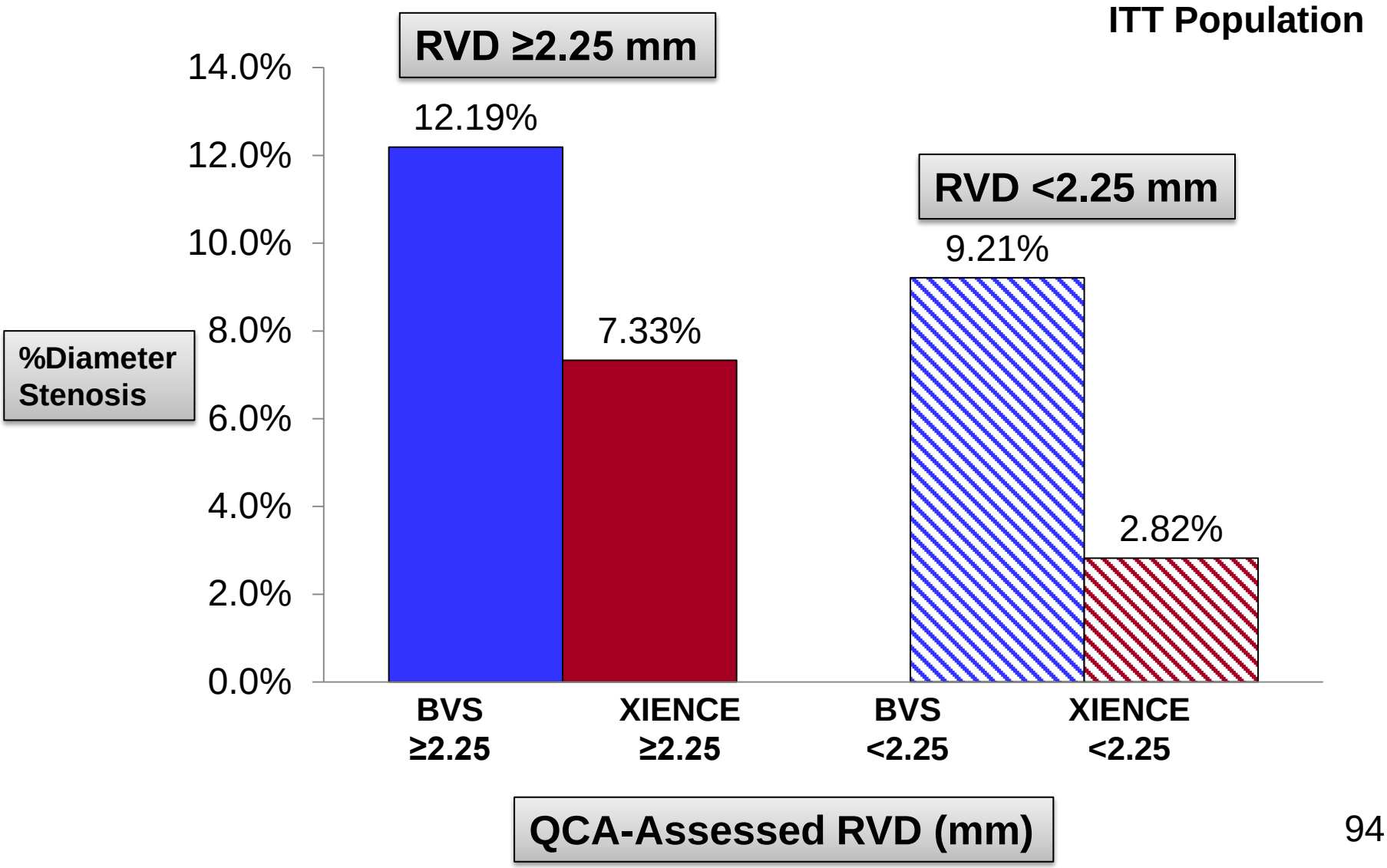
Key Anatomic/Procedural Features Stratified by Vessel Size

	RVD ≥2.25 mm		RVD <2.25 mm	
	BVS	**XIENCE**	**BVS**	**XIENCE**
Post-Pre-Dilatation Measurement by QCA				
RVD (mm)	2.80 ± 0.39	2.80 ± 0.40	2.11 ± 0.26	2.12 ± 0.22
MLD (mm)	1.63 ± 0.44	1.59 ± 0.43	1.24 ± 0.34	1.22 ± 0.30
%DS	41.57 ± 14.37	43.09 ± 13.95	40.73 ± 15.20	41.84 ± 14.34
Post-Scaffold/Stent Implantation Measurement by QCA				
RVD (mm)	2.82 ± 0.39	2.82 ± 0.41	2.15 ± 0.27	2.13 ± 0.23
In-Segment MLD (mm)	2.26 ± 0.37	2.25 ± 0.39	1.72 ± 0.27	1.71 ± 0.25
In-Segment %DS	20.03 ± 7.95	19.90 ± 8.11	20.10 ± 7.95	19.49 ± 8.51
In-Segment Acute Gain (mm)	1.28 ± 0.46	1.30 ± 0.46	1.00 ± 0.36	1.01 ± 0.31

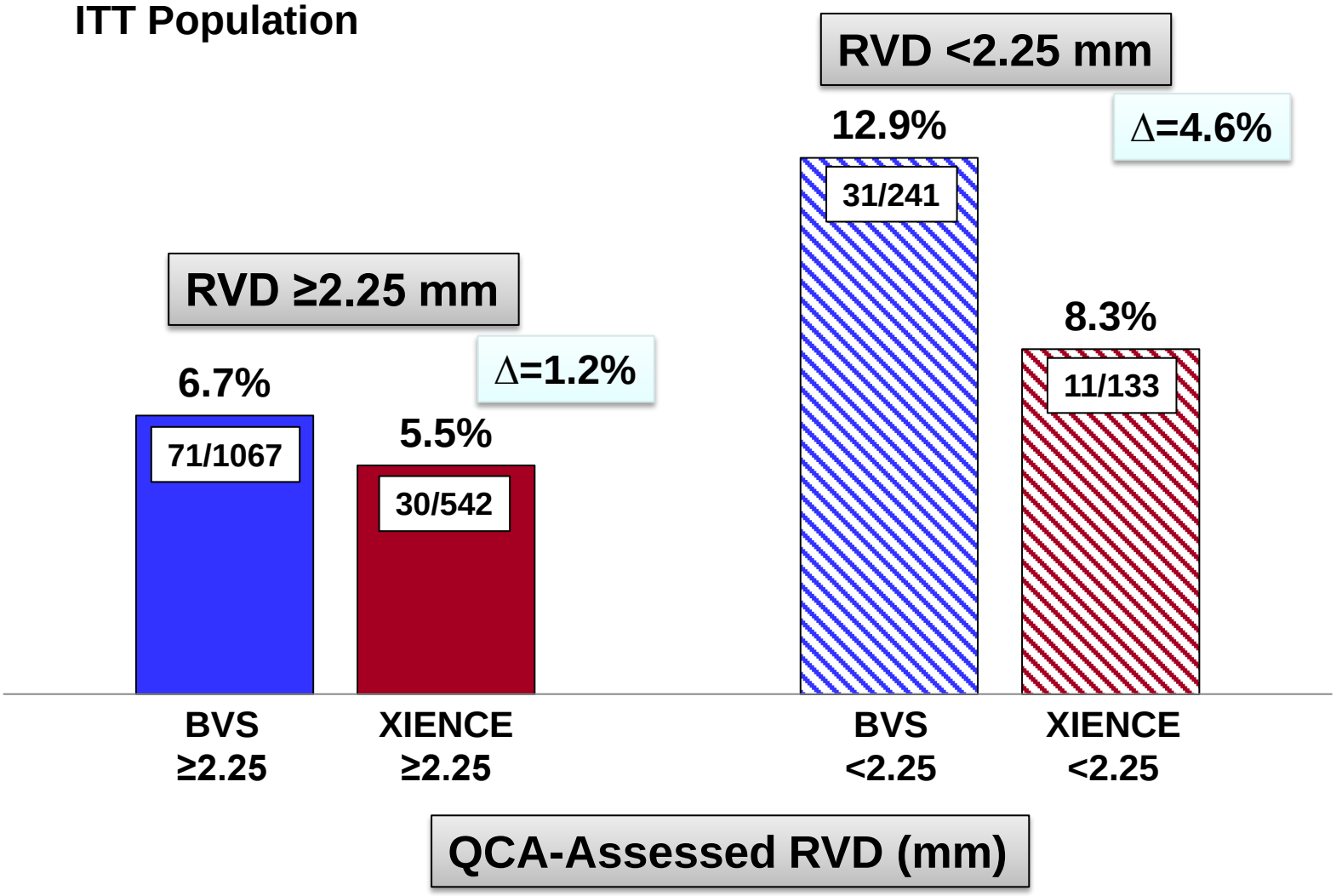
In-Device Post-Implantation Measurements Stratified by QCA RVD



In-Device Post-Implantation Percent Stenosis Stratified by QCA RVD

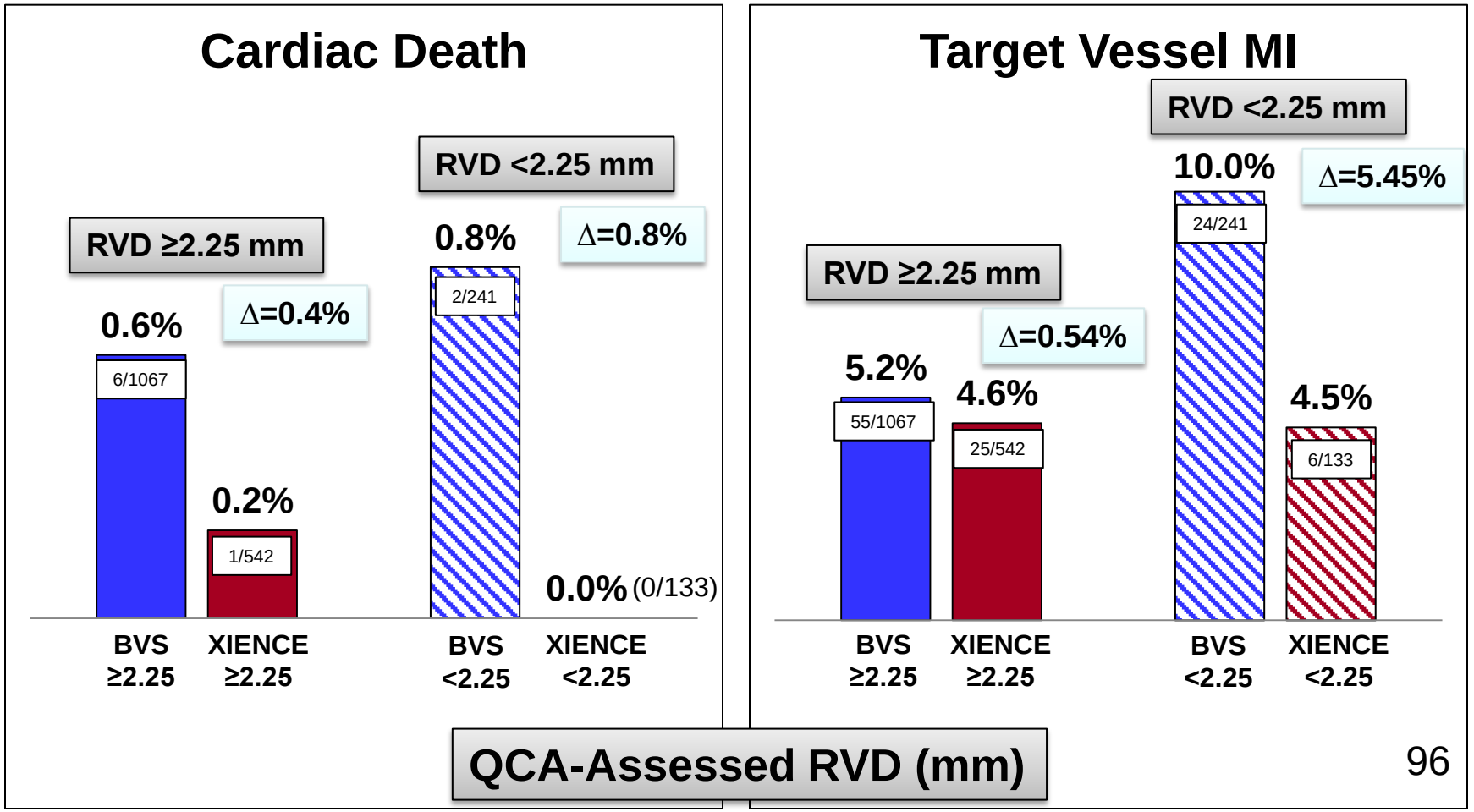


TLF at 1-Year Stratified by QCA-Assessed RVD



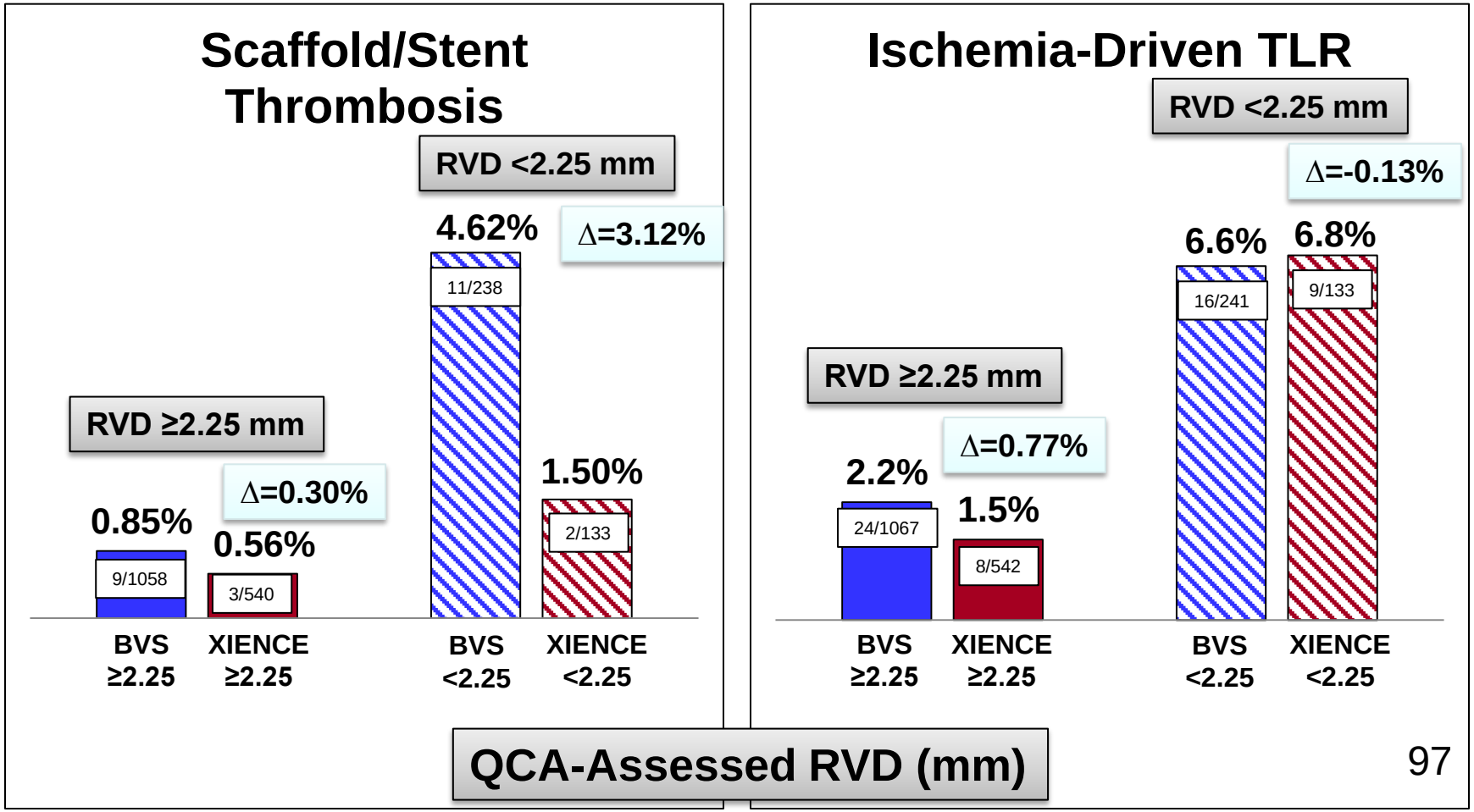
Cardiac Death and Target Vessel MI at 1-Year Stratified by QCA-Assessed RVD

ITT Population



Device Thrombosis and Ischemia-Driven TLR at 1-Year Stratified by QCA-Assessed RVD

ITT Population



TLF at 1-Year in BVS Subjects Stratified by Vessel Size in Non-US Studies

BVS Subjects	Overall ITT Population	RVD ≥2.25 mm	RVD <2.25 mm
ABSORB Cohort B	6.9% (7/101)	5.0% (4/80)	11.8% (2/17)
ABSORB EXTEND	5.0% (41/812)	4.7% (32/675)	5.6% (7/124)
ABSORB II	6.0% (20/331)	5.0% (13/259)	9.7% (7/72)
ABSORB JAPAN	4.2% (11/265)	4.5% (10/223)	2.4% (1/41)
ABSORB III	7.8% (102/1313)	6.7% (71/1067)	12.9% (31/241)

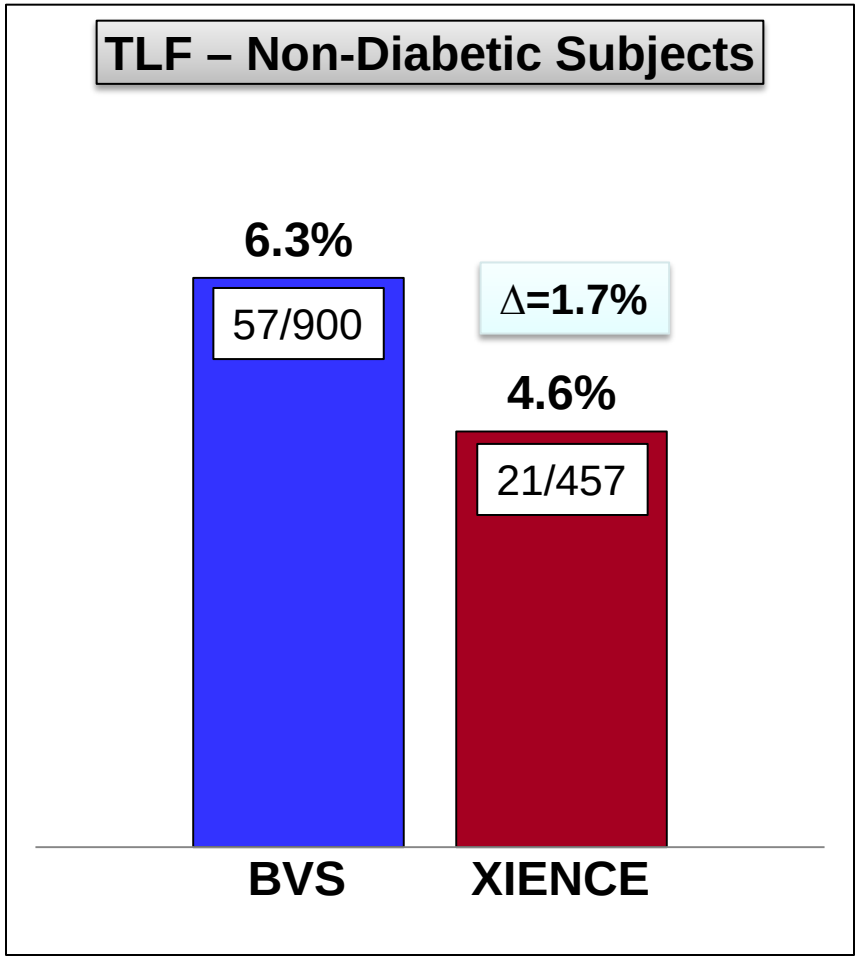
Similar pattern of increased event rates when BVS used in vessels with a QCA-assessed <2.25 mm

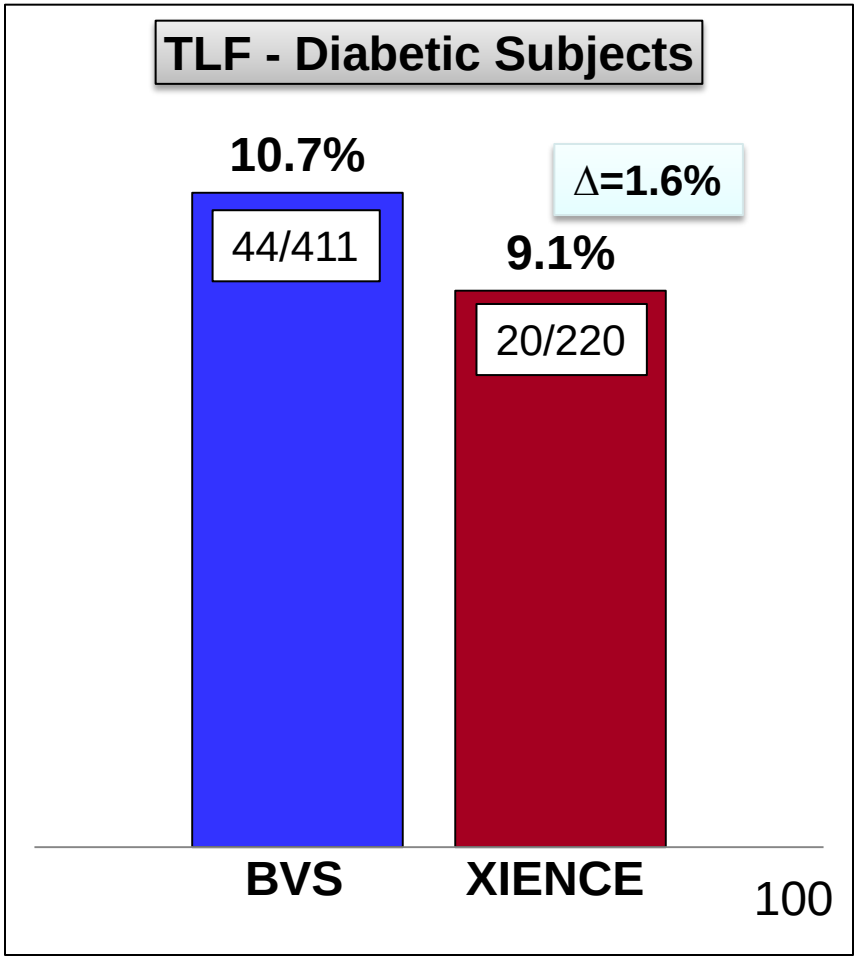
ABSORB III Subjects With Diabetes Mellitus

Post hoc analysis

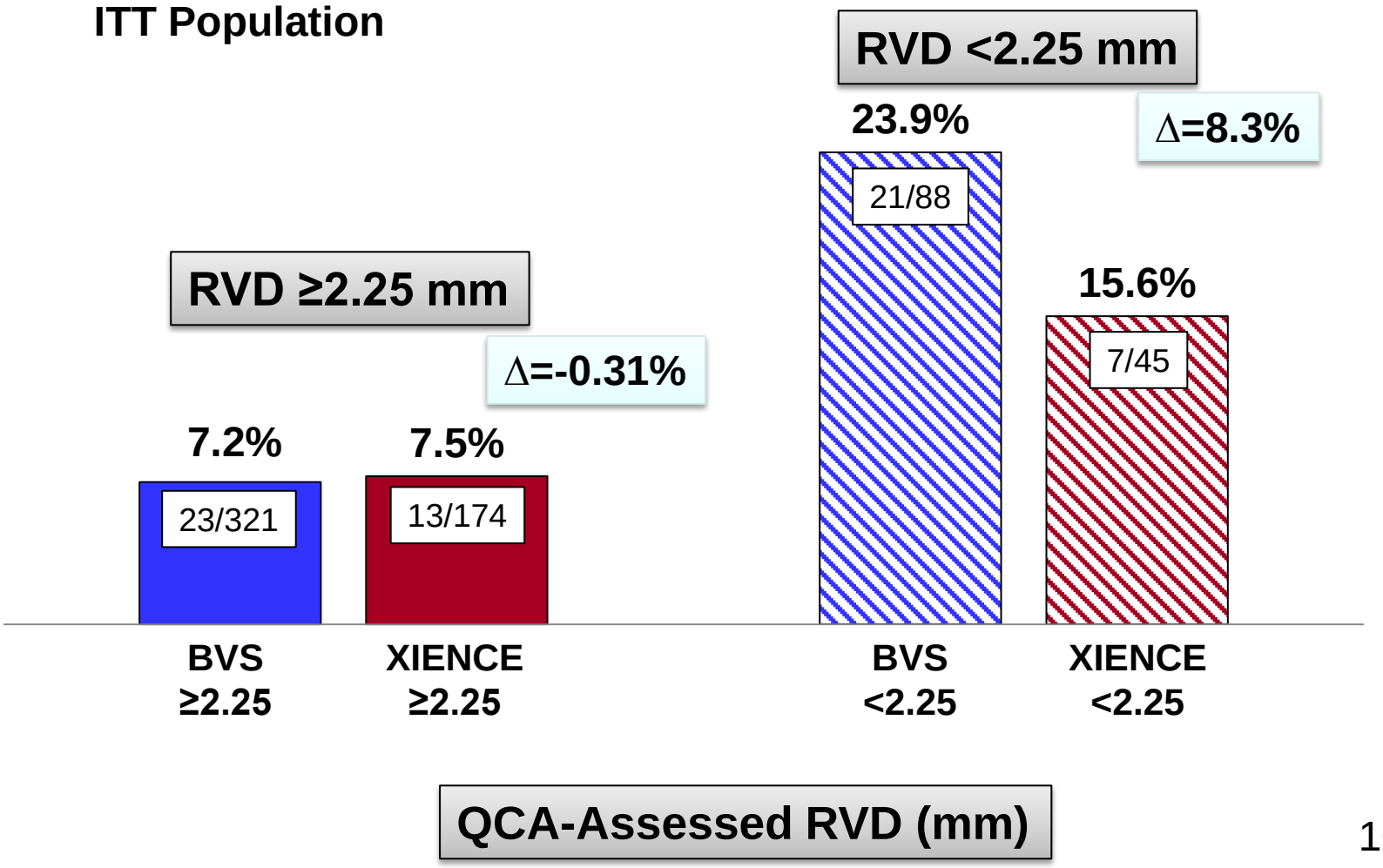
ABSORB III 1-Year TLF in Subjects Without and With Diabetes Mellitus

ITT Population



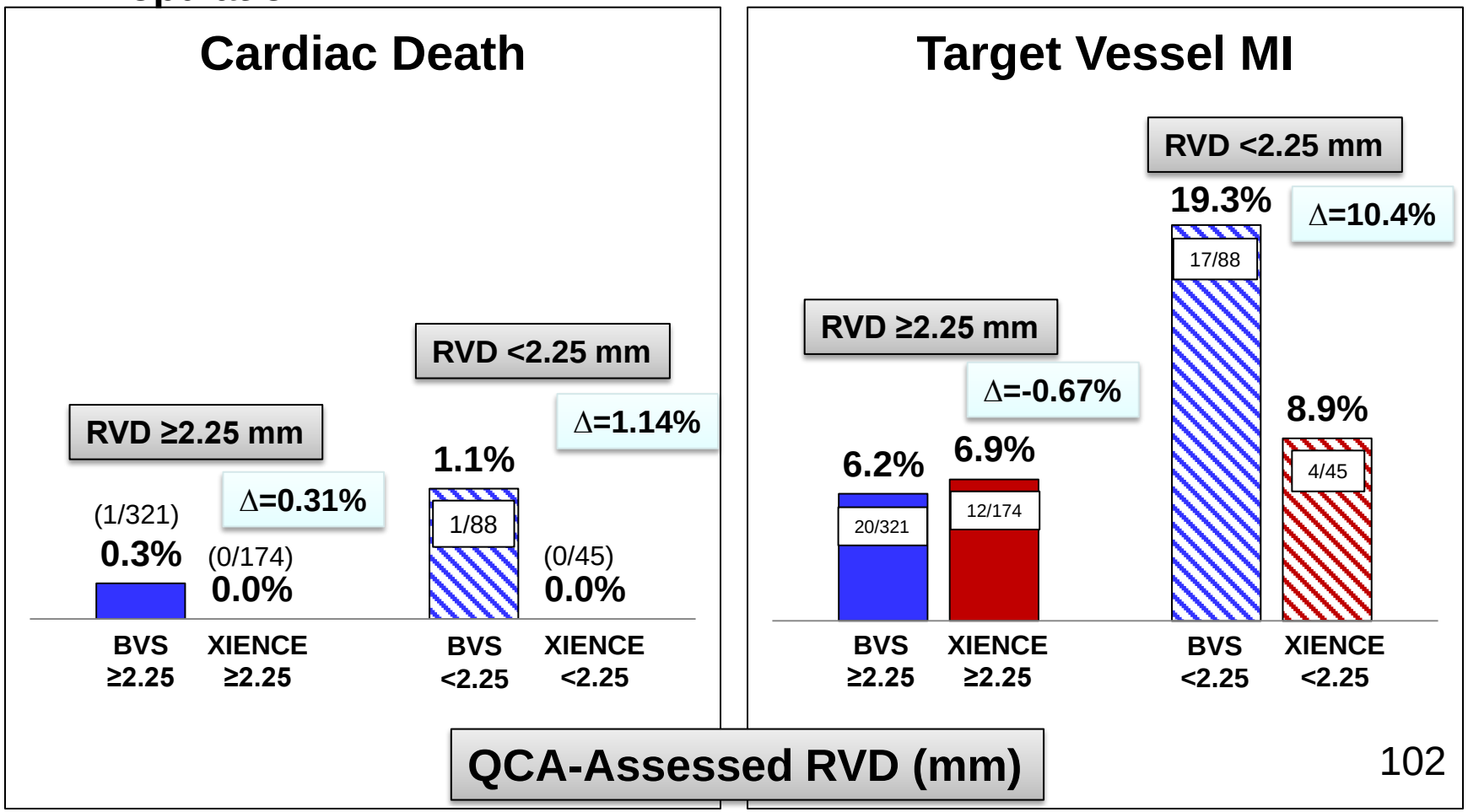


TLF at 1-Year Stratified by QCA-Assessed RVD in Subjects With Diabetes Mellitus



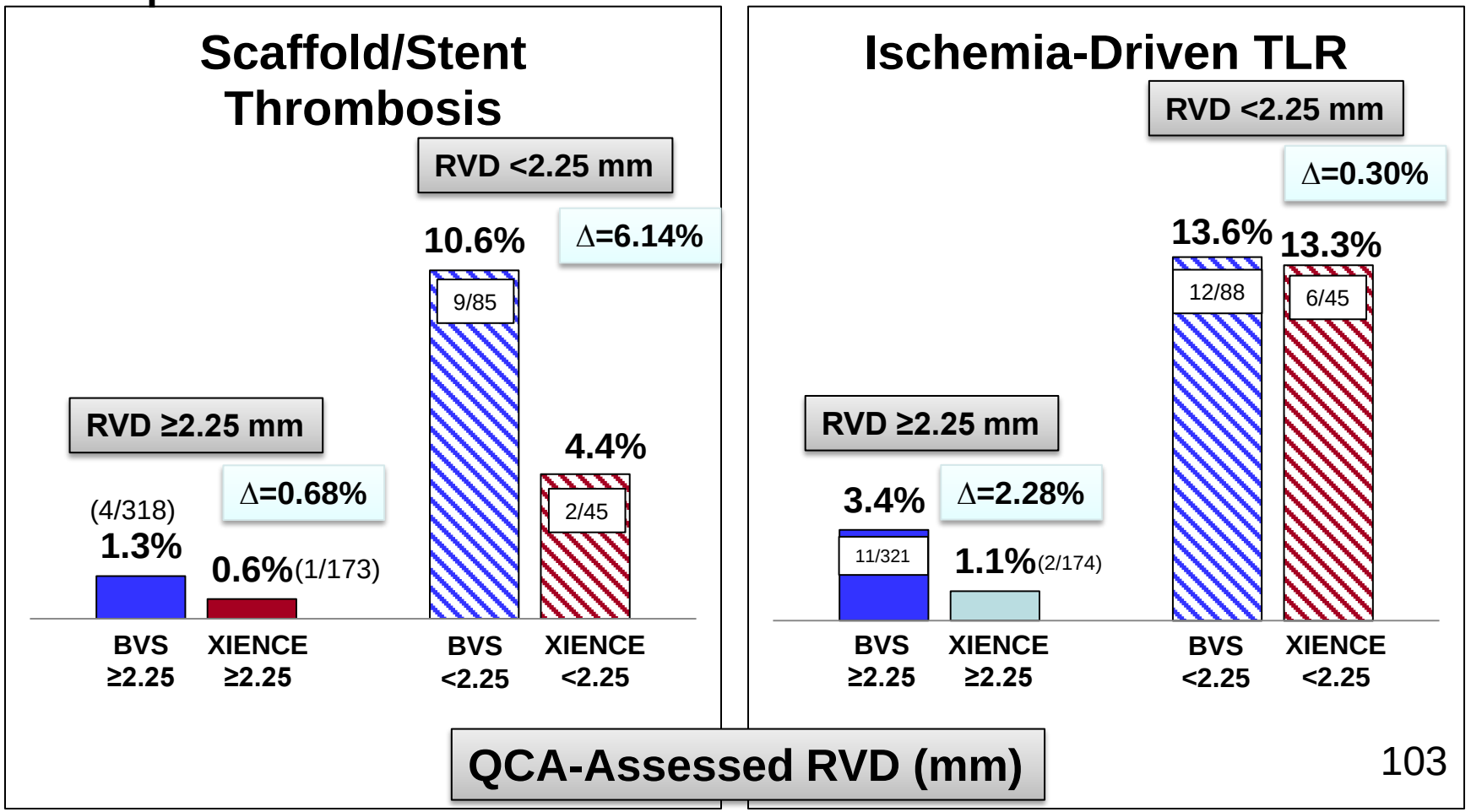
Cardiac Death and Target Vessel MI at 1-Year Stratified by QCA-Assessed RVD in Subjects With Diabetes Mellitus

ITT Population



Device Thrombosis and Ischemia-Driven TLR at 1-Year Stratified by QCA-Assessed RVD in Subjects With Diabetes Mellitus

ITT Population



Labeling Recommendations to Address Vessel Size Selection

Warning: *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.*

Precaution: *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).*

Proportion of ABSORB III Subjects in Which Quantitative Imaging Was Used

	BVS	XIENCE
Quantitative Imaging Used*	11.8% (156/1322)	11.4% (78/686)

***IVUS, OCT, on-line QCA, or angiographic caliper**

Use of Quantitative Imaging in ABSORB III and Enrollment of Subjects With an RVD <2.25 mm

	BVS		XIENCE	
Quantitative Imaging Used	11.8% (156/1322)		11.4% (78/686)	
	(+)Quantitative Imaging (N=156)	**(-)Quantitative Imaging (n=1146)**	**(+)Quantitative Imaging (N=78)**	**(-)Quantitative Imaging (N=595)**
Subjects with RVD <2.25 mm	15.4% (24/156)	18.4% (211/1146)	14.1% (11/78)	20.2% (120/595)

Use of quantitative imaging had a modest impact on the enrollment of subjects with an RVD <2.25 mm

Proportion of Subjects With a QCA-Assessed RVD <2.25 mm in Non-US BVS Studies

	Proportion of Subjects with a Pre-Procedure RVD <2.25 mm
ABSORB Cohort B (N=101)	17.5% (17/97)
ABSORB JAPAN (N=400)	14.5% (58/400)
ABSORB EXTEND (N=812)	15.5% (124/799)
ABSORB II (N=501)	20.4% (102/499)
ABSORB III (N=1998)	18.8 (375/1998)

The enrollment of subjects with an RVD <2.25 mm in non-US BVS studies was generally similar to ABSORB III

Use of Quantitative Imaging and the Enrollment of Subjects With Undersized RVDs: *Observations from Non-US BVS Studies*

ABSORB Cohort B and ABSORB Japan: Quantitative Imaging Optional

	Proportion of Subjects with a Pre-Procedure RVD <2.25 mm
ABSORB Cohort B (N=101)	17.5% (17/97)
ABSORB JAPAN (N=400)	14.5% (58/400)
ABSORB EXTEND (N=812)	15.5% (124/799)
ABSORB II (N=501)	20.4% (102/499)

Use or Non-Use of Quantitative Imaging: Observations from Non-US BVS Studies

ABSORB EXTEND and ABSORB II:
Quantitative Imaging Required Per Protocol

	Proportion of Subjects with a Pre-Procedure RVD <2.25 mm
ABSORB Cohort B (N=101)	17.5% (17/97)
ABSORB JAPAN (N=400)	14.5% (58/400)
ABSORB EXTEND (N=812)	15.5% (124/799)
ABSORB II (N=501)	20.4% (102/499)

Use or Non-Use of Quantitative Imaging: Observations from Non-US BVS Studies vs. ABSORB III

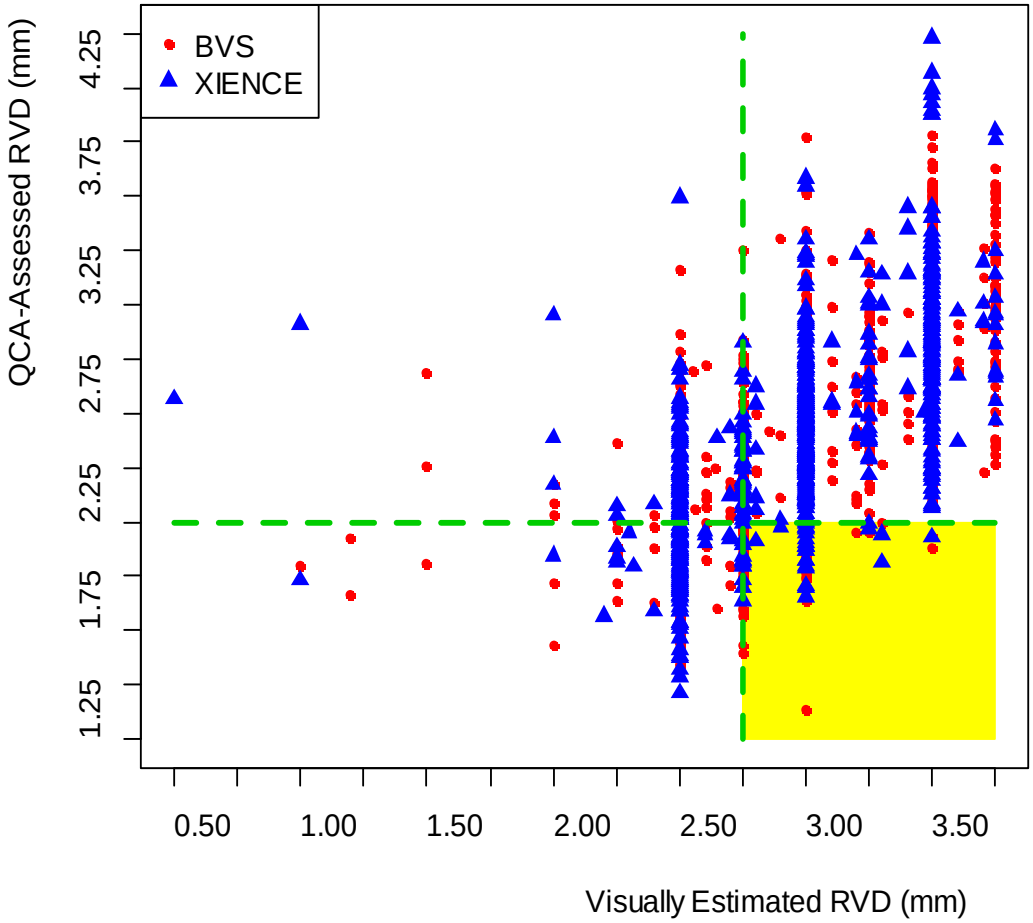
ABSORB III:
Quantitative Imaging Optional

	Proportion of Subjects with a Pre-Procedure RVD <2.25 mm
ABSORB Cohort B (N=101)	17.5% (17/97)
ABSORB JAPAN (N=400)	14.5% (58/400)
ABSORB EXTEND (N=812)	15.5% (124/799)
ABSORB II (N=501)	20.4% (102/499)
ABSORB III (N=1998)	18.8 (375/1998)

Assessing the Proposed Vessel Size Precaution

Precaution: 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).

Scatter Plot of Visually-Assessed RVD vs. ABSORB III QCA-Assessed RVD



	RVD (QCA) <2.25 mm (N=375)
Visual RVD >2.5 mm	31.5% (118/375)
Visual RVD >2.75 mm	**17.3% (65/375)**
Visual RVD >3.00 mm	2.4% (9/375)

Sponsor Recommendations for BVS Post-Dilatation

Sponsor Recommendations for Post-Dilatation in the Instructions For Use:

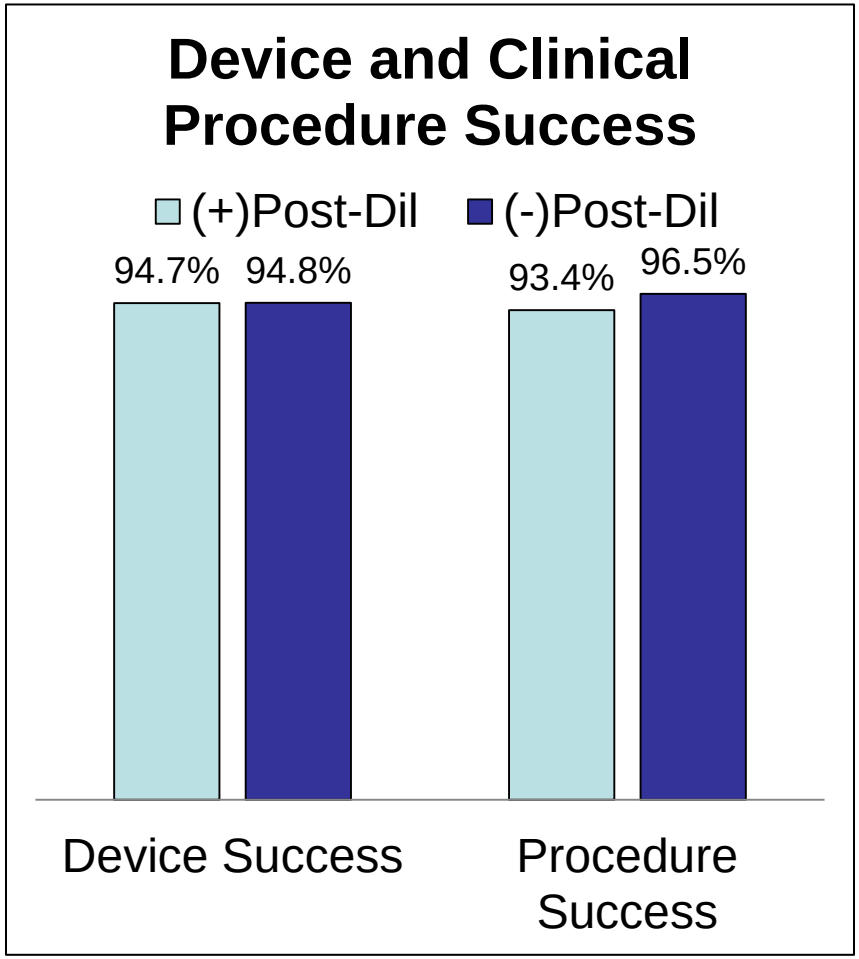
> *Precaution: Post-dilatation is strongly recommended for optimal scaffold apposition. When performed, post-dilatation should be at high pressure with a non-compliant balloon.*

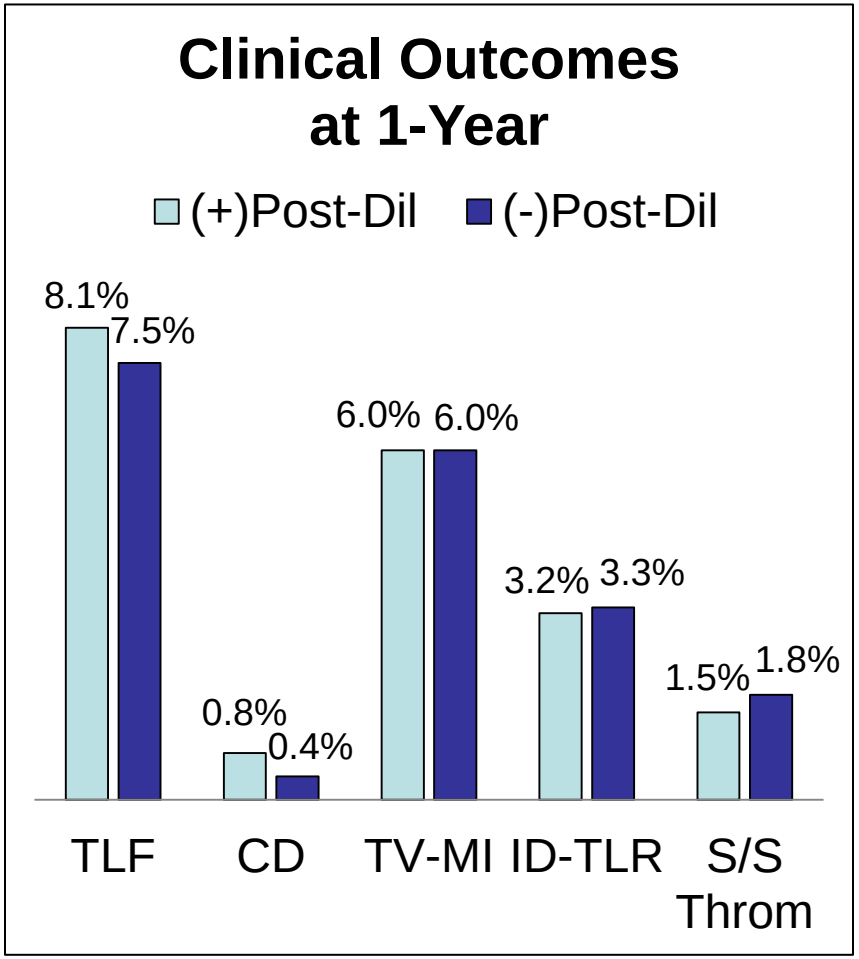
BVS Post-Dilatation in ABSORB III

Post-dilatation with a non-compliant balloon was left up to the discretion of the operator

BVS	(+)Post-Dilatation	(-)Post-Dilatation
Subjects (n=1219)	62.8% (765/1219)	37.2% (454/1219)
Lesions (n=1276)	63.4% (809/1276)	36.6% (467/1276)

BVS Post-Dilatation in ABSORB III





Post-dilatation performed with a non-compliant balloon

Interpretation of ABSORB III BVS Post-Dilatation Data

- There was no evidence of higher device or procedure success rates, or 1-year clinical outcomes when post-dilatation was performed.
- However, the following should be considered when interpreting these data:
  - Post-hoc analysis
  - Subjects were not randomized to post-dilatation versus no post-dilatation.
  - The reasons for post-dilatation could have been based on lesion complexity or technical issues during the index procedure

FDA Perspectives on the Small Vessel Analysis and Whether Appropriately-Sized Vessels Can be Selected for Safe BVS Use

- Nearly 20% of ABSORB III subjects had a target vessel with a QCA-assessed RVD of <2.25 mm.
- There was a clear signal for increased event rates when a BVS is placed in small vessels.
  - This signal was more pronounced in subjects with diabetes mellitus and small vessels.

FDA Perspectives on the Small Vessel Analysis

- To guide operators on selecting patients with appropriately-sized vessels for BVS implantation, the sponsor recommends that on-line QCA or intravascular imaging be used if the visually-assessed RVD is believed to be *≤2.75 mm.*
  - The rates of BVS implantation in vessels with a QCA-assessed RVD <2.25 mm were generally similar irrespective of whether quantitative imaging modalities were used at the operator's discretion (ABSORB III, ABSORB COHORT B, and ABSORB Japan) or used per protocol (ABSORB Extend and ABSORB II).
    - Operators in these studies were not aware of the BVS performance in small vessels at the time of the index procedure.

FDA Perspectives on BVS Post-Dilatation

- For optimal BVS implantation, the sponsor recommends post-dilatation with a non-compliant balloon.
- In a post-hoc analysis (with methodological limitations), BVS post-dilatation was not associated with higher device or clinical procedure success rates, or 1-year clinical outcomes.

The ABSORB BVS Family of Studies

Supplementary non-US BVS studies submitted to support BVS safety and effectiveness

The ABSORB BVS Family of Studies

Non-US Studies

- ABSORB Cohort B Study
  - 101 BVS
- ABSORB EXTEND Study
  - 812 BVS
- ABSORB II Randomized Trial
  - 335 BVS, 166 XIENCE
- ABSORB Japan Randomized Trial
  - 266 BVS, 134 XIENCE

US Study

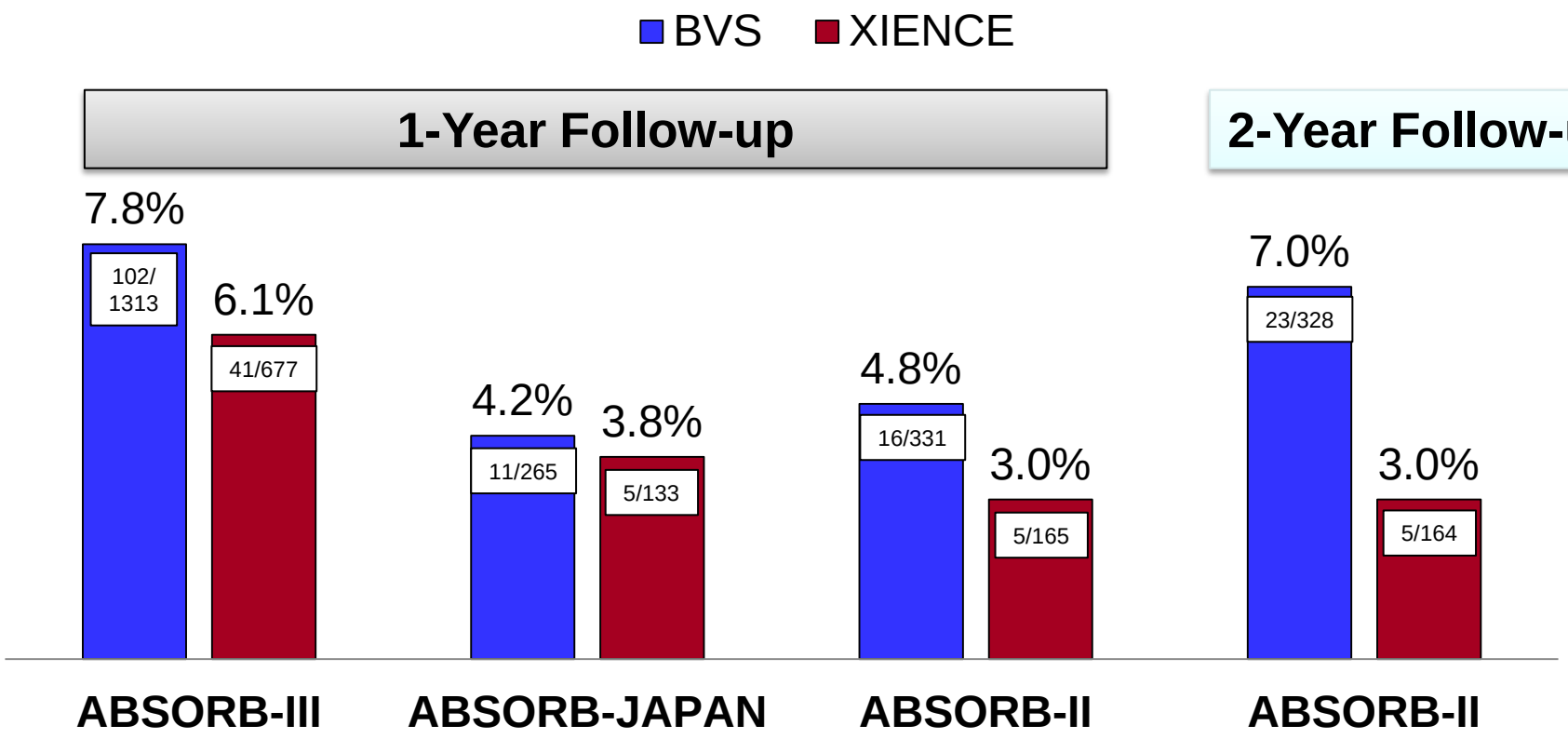
- ABSORB III Randomized Trial
  - 1322 BVS, 686 XIENCE

Latest Available Clinical Follow-Up of BVS Study Subjects

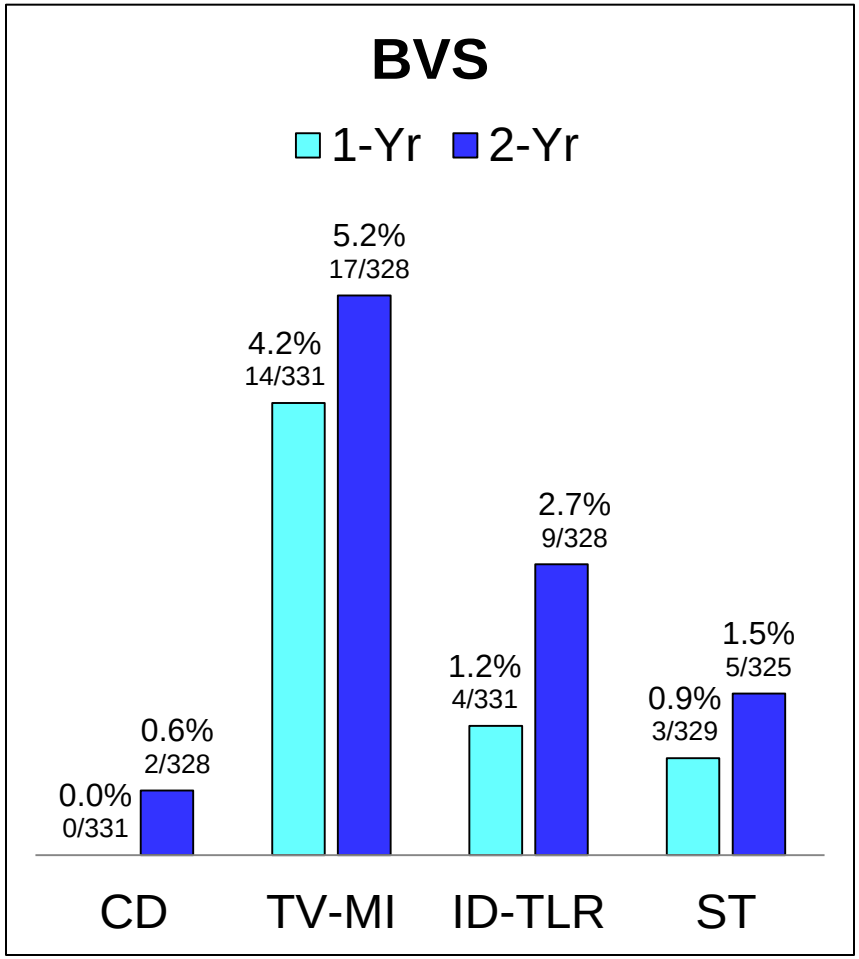
	1 Year	2 Years	3 Years	4 Years	5 Years
ABSORB Cohort B	101	100	100	100	100
ABSORB Extend	811	807	613		
ABSORB II	331	328			
ABSORB Japan	265				
ABSORB III	1313				
Total	**2821**	**1235**	**713**	**100**	**100**

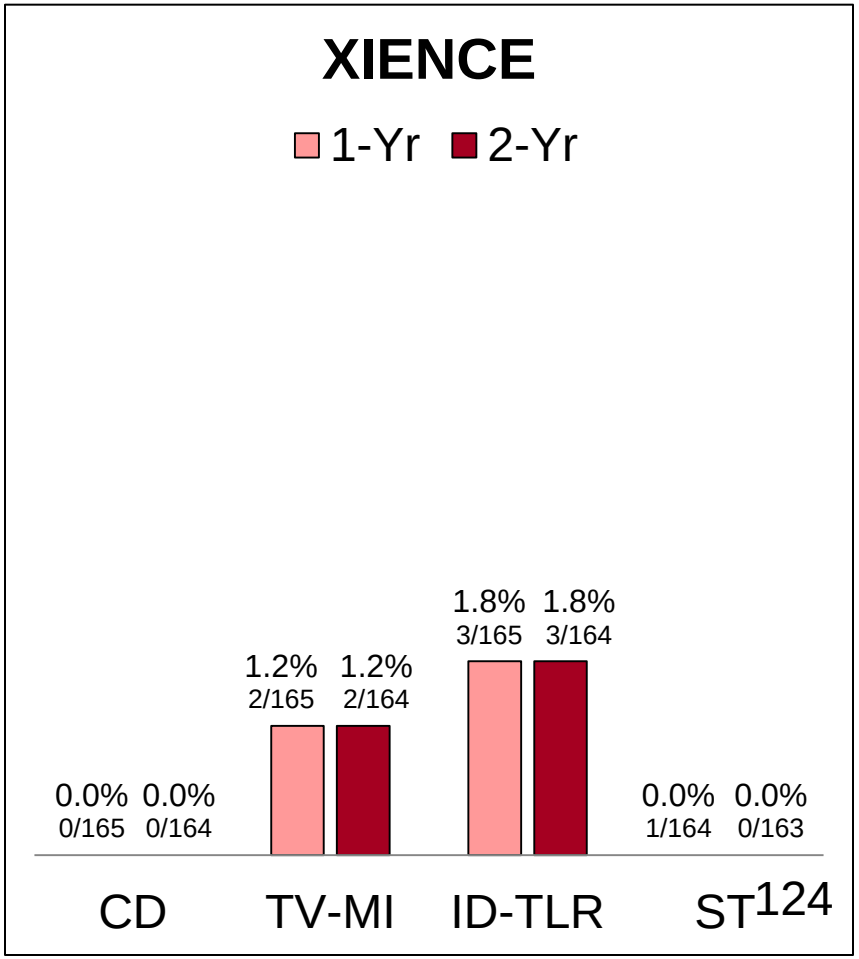
ABSORB BVS Family of Studies Randomized Trials

Target Lesion Failure at 1 and 2 Years

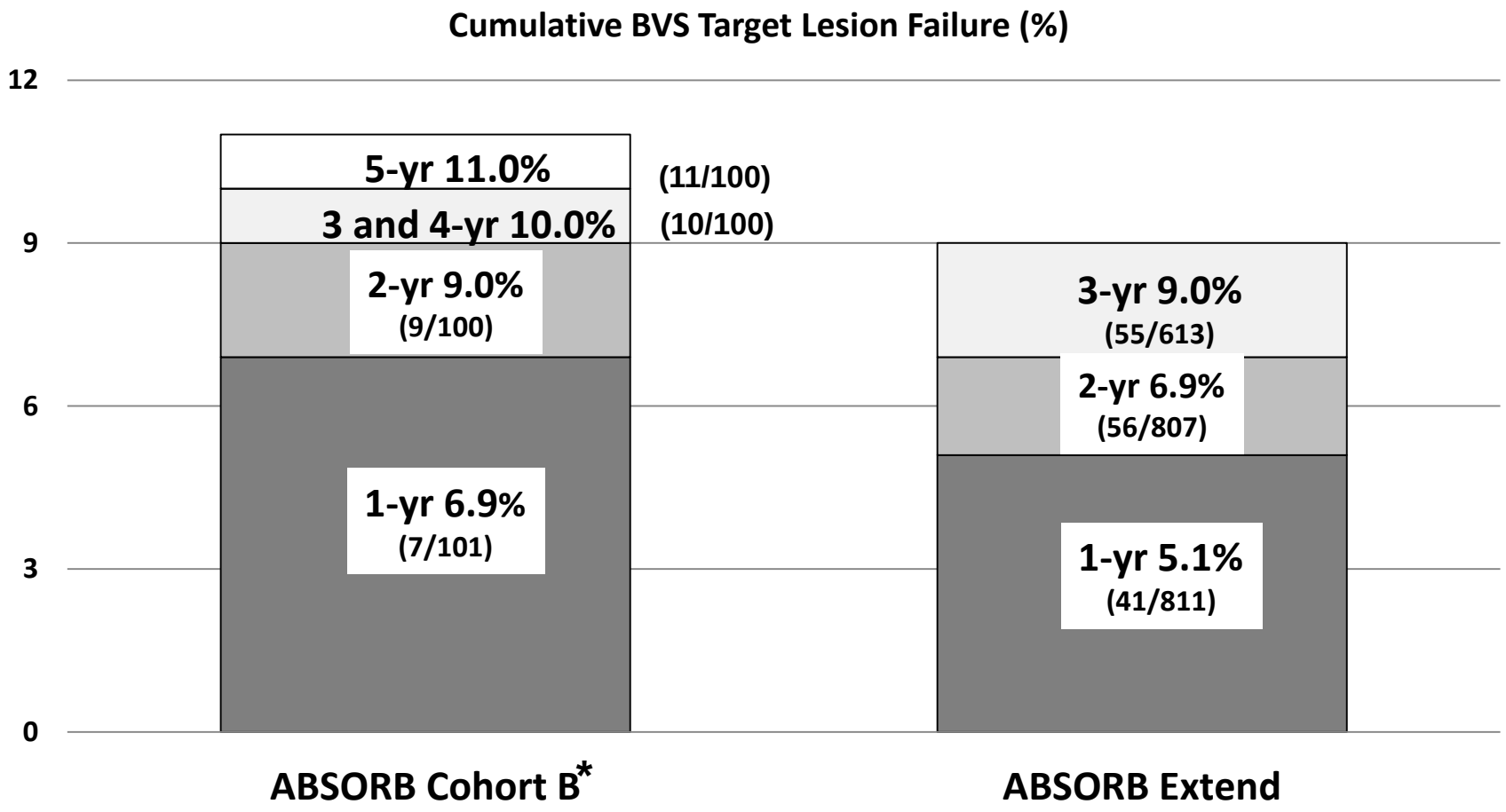


ABSORB II 1 and 2-Year Cardiovascular Outcomes



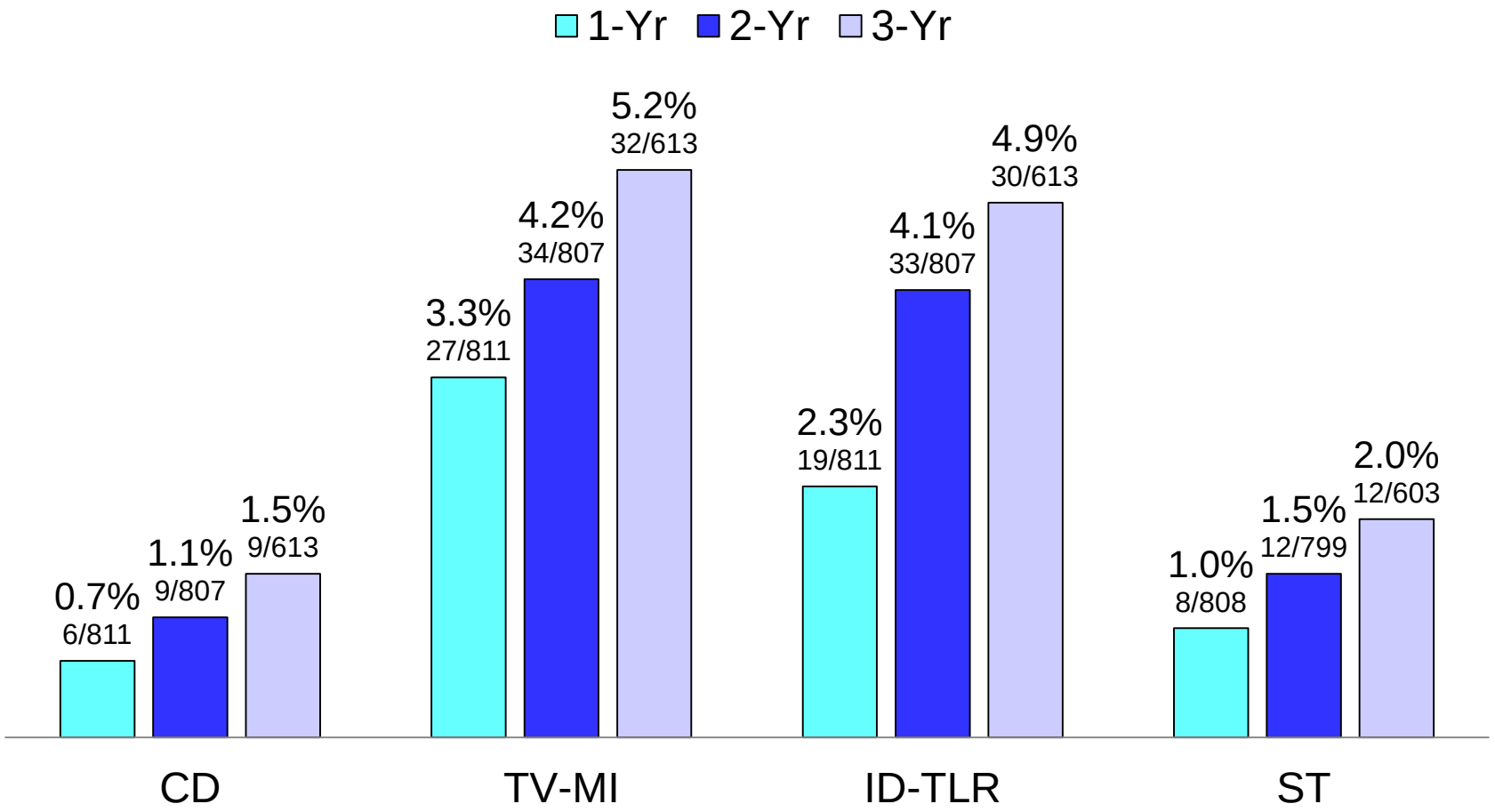


ABSORB BVS Program Single Arm Studies



*All Cohort B subjects received a single 3.0 x 18 mm BVS

ABSORB Extend 1, 2 and 3-Year Cardiovascular Outcomes



FDA Perspectives on the ABSORB BVS Family of Studies

- The observed 1-year TLF rates in patients implanted with the BVS ranged from 4.2% in ABSORB Japan to 7.8% in ABSORB III.
- Across the randomized trials (ABSORB III, ABSORB Japan, and ABSORB II), there is a consistent signal of an increased observed event rate in the BVS group vs. XIENCE at 1-year ranging from 0.4% to 1.8%.
  - Two-year follow-up randomized data are limited to ABSORB II (335 BVS vs. 166 XIENCE subjects), which showed a modest 2.2% increase in TLF between year 1 and year 2 in the BVS group.

Clinical Review Summary Comments (1)

- The BVS is a first-of-a kind fully absorbable drug-eluting coronary scaffold.
- In the pivotal ABSORB III trial, the BVS met its 1-year TLF primary endpoint for non-inferiority vs. the XIENCE stent.
  - In the ITT population, the observed difference in the 1-year TLF rate was 1.7% (BVS rate greater than XIENCE), which increased to 1.9% and 2.1% in the As-Treated and PTE populations, respectively.

Clinical Review Summary Comments (2)

- In ABSORB III through 1-year:
  - For safety (risks), the observed rates of cardiac death and target vessel MI and scaffold/stent thrombosis were numerically higher in the BVS group.
    - The scaffold/stent thrombosis rate was >2-fold higher in the BVS group vs. the Xience group.
  - For effectiveness (benefits):
    - The observed rates of ischemia-driven TLR were similar between treatment groups.
    - There was no superiority signal of the BVS vs. XIENCE for the 1-year rates of angina, all revascularization, or ID-TVR.

Clinical Review Summary Comments (3)

- There was a clear signal for increased cardiac safety events when a BVS was placed in small vessels.
  - This signal was more pronounced in diabetic subjects who underwent implantation of a BVS in small vessels.
  - The sponsor has proposed to mitigate these risks *in the post-market setting* via operator training and labeling precautions and warnings aimed to:
    - Select patients with appropriately-sized target vessels for BVS use.
    - Optimize deployment with BVS post-dilatation.

Clinical Review Summary Comments (4)

- One-year cardiac outcomes in BVS-treated subjects enrolled in the non-US ABSORB family of studies are generally consistent with the ABSORB III trial.
- There are no worrisome safety or effectiveness signals in longer-term follow-up of BVS subjects, but data (particularly data from randomized trials) are limited.

FDA Presentations

- Introduction and Regulatory History
  Dr. Kenya Brothers
- Statistical Presentation
  Dr. Yu Zhao
- Clinical Presentation – Overview
  Dr. Adrian Magee
- Clinical Presentation – Clinical Results
  Dr. Andrew Farb
- Post-Approval Considerations
  Dr. Nadezda Radoja
- Summary
  Dr. Kenya Brothers

Post-Approval Considerations

Nadezda Radoja, Ph.D.
Division of Epidemiology
Office of Surveillance and Biometrics

Disclaimer

- The discussion of a Post-Approval Study (PAS) prior to a formal recommendation on the approvability of this PMA should not be interpreted to mean that FDA is suggesting the Panel find the device approvable.
- The plan to conduct a PAS does not decrease the threshold of evidence required to find the device approvable.
- The premarket data submitted to the Agency and discussed today must stand on its own in demonstrating a reasonable assurance of safety and effectiveness in order for the device to be found approvable.

Post-market Conditions of Approval

- Additional non-clinical/bench testing
- Extended follow-up of premarket cohort
- New patient data collection to refine benefit-risk profile
  - Traditional discrete post-approval study
  - Comprehensive registry-based surveillance with shared responsibilities

Issues Specific to BVS

- Long-term follow-up of BVS patients
- The effectiveness of a new operator training program for optimal BVS use in newly enrolled patients.
- BVS performance in sub-groups.
- No outstanding non-clinical testing concerns need to be addressed post-market

Sponsor's Proposed Post-Approval Study Plan:

1. Continue ABSORB III follow-up through 5 years
2. New Enrollment
   - 2,000 – 3,000 patients
   - 150 - 200 sites
   - Broader patient population and physicians
   - Analyze low frequency events
   - Imaging sub-group to evaluate effectiveness of labeling and training to select for proper size arteries
   - 5-year follow-up of safety and effectiveness outcomes

FDA Assessment of Post-Approval Study Plan

- Postmarket plan requires further development
  - Extended follow-up is common approach
  - Registry-based surveillance used in other devices
  - Traditional Discrete study may also be appropriate
- Panel:
  - Additional input required to determine whether proposal will be capable of addressing issues identified by FDA

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- Summary
  Dr. Kenya Brothers

FDA Summary

- No outstanding concerns related to non-clinical testing
- BVS demonstrated statistical non-inferiority to XIENCE in primary endpoint (1-year TLF)
- Rates of safety events (cardiac death, MI, ID-TLR, ST) numerically higher in BVS group
  - >2-fold increase in device thrombosis in BVS group
- Increased incidences of safety events in small vessels
- Did not demonstrate superiority for powered secondary endpoints (angina at 1 year, all revascularizations, ID-TVR)

Absorb GT1™ Bioresorbable Vascular Scaffold (BVS) System

FDA Review of P150023

Panel Questions

Question 1
Safety and Effectiveness

The BVS met its non-inferiority endpoint for 1-year TLF. The absolute difference of the TLF rate between the BVS and XIENCE treatment groups favored the XIENCE group by 1.71%.

The rates of the individual components of TLF (most notably target vessel MI) and definite plus probable stent thrombosis were numerically higher in the BVS group vs. the XIENCE group.

Question 1
Safety and Effectiveness

Please comment on whether the ABSORB III results provide adequate evidence of clinical non-inferiority of the BVS as compared to the XIENCE stent with regard to (A) safety and (B) effectiveness in the patient population described by the proposed indications for use.

Question 2
BVS Use in Small Coronary Arteries

In the ABSORB III trial, a target vessel size inclusion criterion was a reference vessel diameter (RVD) determined following pre-dilatation of ≥2.5 mm (as visually assessed by the operator). Visual estimates of coronary artery dimensions typically overestimate true vessel diameters as measured by angiographic core labs using quantitative coronary angiography (QCA).

In both treatment groups, event rates were higher in subjects with a QCA-assessed RVD <2.25 mm as compared with a ≥2.25 mm RVD. However, except for ID-TLR, the event rate differences between the BVS group and the XIENCE group were greater in subjects with a <2.25 mm RVD treated artery (most notably for rates of TLF, target vessel MI and scaffold/stent thrombosis).

Question 2
BVS Use in Small Coronary Arteries

Please comment on the clinical significance of the higher event rates observed when a BVS was implanted in an artery with a QCA-assessed RVD of <2.25 mm.

Question 3
BVS Use in Small Coronary Arteries

The sponsor proposed the following precaution and warning for the Absorb GT1 BVS Instructions For Use:

Precaution: *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).*

Warning: *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.*

Question 3a
BVS Use in Small Coronary Arteries

Please comment on the adequacy of the proposed Precaution to recommend that operators utilize on-line QCA or intravascular imaging to confirm that the target vessel is appropriately sized for safe and effective use of a BVS.

In your deliberations, please also consider whether the BVS clinical data and operator expertise adequately support the proposed visually-assessed ≤2.75 mm diameter threshold for the use of quantitative imaging to confirm the selection of appropriately sized vessels for scaffold implantation.

Question 3b
BVS Use in Small Coronary Arteries

Please comment on the adequacy of the proposed Warning against the use of a BVS in vessels with an RVD <2.5 mm.

Question 4
BVS Use in Small Coronary Arteries

The event rate differences between the BVS group and the XIENCE group were more pronounced in subjects with diabetes mellitus and a QCA-assessed <2.25 mm RVD treated artery (most notably for the rates of TLF, target vessel MI, and scaffold thrombosis) compared with diabetic subjects with a ≥2.25 mm RVD.

Question 4
BVS Use in Small Coronary Arteries

Please comment on whether or not the Instructions For Use should include additional language regarding an increased risk for adverse events when a BVS is implanted in small vessels (angiographic core lab-assessed RVD <2.25 mm) in patients with diabetes mellitus.

Question 5
Duration of Follow-up

	1 Year	2 Years	3 Years	4 Years	5 Years
ABSORB Cohort B	101	100	100	100	100
ABSORB EXTEND	811	807	613		
ABSORB II	331	328			
ABSORB Japan	265				
ABSORB III	1313				
Total	**2821**	**1235**	**713**	**100**	**100**

In the ABSORB III pivotal study, the BVS met its non-inferiority endpoint for the rate of TLF at 12 months but with the caveats as presented in Question 1. There are additional clinical outcomes data for BVS patients from other non-US studies to supplement the ABSORB III results.

Question 5
Duration of Follow-up

Please comment on whether or not the PMA includes adequate follow-up data in a sufficient portion of the patient population identified in the proposed indications to support a reasonable assurance of safety and effectiveness.

If the duration of follow-up is insufficient, please comment on how much additional follow-up data from the ABSORB III trial should be provided to demonstrate a reasonable assurance of BVS safety and effectiveness.

Question 6
BVS Post-Dilatation

The BVS Instructions For Use includes the following statement in the Precautions section:

> ***Precaution:*** *Post-dilatation is strongly recommended for optimal scaffold apposition. When performed, post-dilatation should be at high pressure with a non-compliant balloon.*

In the ABSORB III BVS group, post-dilatation was performed in 64.8% of lesions. The rate of BVS implantation procedural success was slightly lower when post-dilatation was performed; and post-dilatation was not associated with a consistent improvement in the 1-year rates of TLF, cardiac death, target vessel MI, ischemia-driven TLF and scaffold thrombosis.

Question 6
BVS Post-Dilatation

Please discuss the adequacy of the ABSORB III trial data to support a strong recommendation that post-dilatation should be performed when implanting a BVS.

Question 7
Post-Approval Commitments

The sponsor provided the following post-approval commitments:

- Continue ABSORB III subject follow-up through 5 years
- Conduct a post-approval study in 2,000 – 3,000 newly enrolled patients
  - Approximately 150 – 200 sites
  - Broader patient population and new physicians
  - Analyze low frequency events
  - Imaging sub-group to evaluate effectiveness of labeling and training for small vessel (<2.5 mm) enrollment
  - 5 year follow-up of safety and effectiveness outcomes

Question 7
Post-Approval Commitments

Please comment on any additional study objectives or design features that you recommend for the post-approval study and whether or not the sponsor's post-approval commitments are appropriate.

Question 8
Labeling

Please comment on the proposed contraindications, warnings and precautions in the labeling.

Absorb GT1™ Bioresorbable Vascular Scaffold (BVS) System

FDA Review of P150023

Voting Questions

Voting Question 1

Is there reasonable assurance that the Absorb GT1 Bioresorbable Vascular Scaffold System is safe for use in patients who meet the criteria specified in the proposed indication?

Voting Question 2

Is there reasonable assurance that the Absorb GT1 Bioresorbable Vascular Scaffold System is effective for use in patients who meet the criteria specified in the proposed indication?

Voting Question 3

Do the benefits of the Absorb GT1 Bioresorbable Vascular Scaffold System outweigh the risks for use in patients who meet the criteria specified in the proposed indication?