Everolimus-eluting Bioresorbable Vascular Scaffolds in Patients with Coronary Artery Disease:

The ABSORB III trial

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on behalf of Dean J. Kereiakes, Stephen G. Ellis, D. Christopher Metzger, Ronald P. Caputo, David G. Rizik, Paul S. Teirstein, Marc R. Litt, Annapoorna Kini, Ameer Kabour, Steven O. Marx, Jeffrey J. Popma, Robert McGreevy, Zhen Zhang, Charles Simonton, and the ABSORB III Investigators

ABSORB III

Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Consultant	• Reva Corp.
• Study chairman (uncompensated)	• Abbott Vascular

Absorb BVS

Everolimus/PDLLA (1:1) matrix coating

- 7 µm
- Conformal coating
- Controlled drug release similar to Xience CoCr-EES

PLLA Backbone

- Semi-crystalline
- Circumferential sinusoidal rings connected by linear links
- Strut thickness 150 µm
- Platinum markers in each end ring

Absorb Program Objectives

- Demonstrate similar (non-inferior) results with ABSORB BVS compared to Xience CoCr-EES at 1 year
- Demonstrate superior results compared to Xience CoCr-EES between 1 and 5 years

ABSORB III Study Design

Prospective, multicenter, single-blind, trial
~2,000 patients randomized
2:1 Absorb BVS vs. Xience CoCr-EES

Clinical follow-up:

No routine angiographic follow-up

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

Major Endpoints at 1 Year

Primary Endpoint: Target Lesion Failure (non-inferiority)

- Cardiac death, or
- Myocardial infarction attributed to the target vessel (TV-MI), or
  - Peri-procedural MI: CK-MB >5x ULN w/i 48 hours
- Ischemia-driven target lesion revascularization (ID-TLR)

Powered Secondary Endpoints (superiority)

- Angina
- All revascularization
- Ischemia-driven target vessel revascularization (ID-TVR)

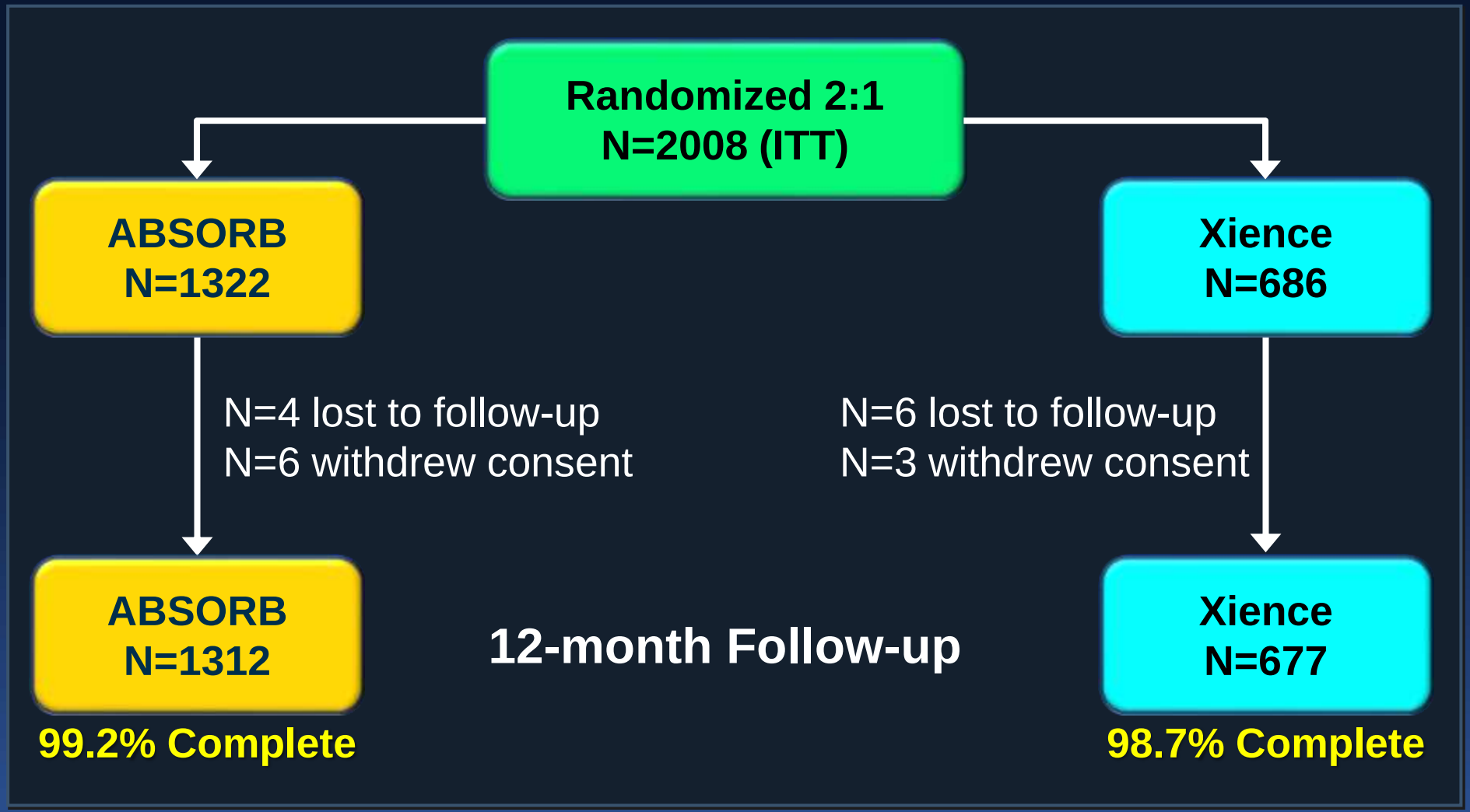
Ellis SG et al. N Engl J Med. 2015;373:1905-15

Key Patient Eligibility Criteria

- >18 years old
- Evidence of myocardial ischemia (stable/unstable/post-infarction angina or silent ischemia)
- No elevation of CK-MB
- 1 or 2 *de novo* target lesions in up to 2 native coronary arteries (max 1 lesion per artery)
- Diameter stenosis ≥50% and <100% with TIMI flow ≥1
  - If <70%, abnormal functional test (including FFR ≤0.80), unstable angina or post-infarct angina
- RVD ≥2.50 mm and ≤3.75 mm (site-determined)
- Lesion length ≤24 mm (site-determined)

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

Study Flow and Follow-up



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

193 Enrolling Centers

tct2015

Post-procedural QCA

Measurement	Absorb (N=1322) (L=1385)	Xience (N=686) (L=713)	p-value
RVD	2.70 ± 0.45	2.68 ± 0.47	0.33
In-Device			
MLD	2.37 ± 0.40	2.49 ± 0.40	<0.0001
Acute gain	1.45 ± 0.45	1.59 ± 0.44	<0.0001
%DS	11.6 ± 8.77	6.4 ± 8.91	<0.0001
In-Segment			
MLD	2.15 ± 0.41	2.14 ± 0.43	0.58
Acute gain	1.23 ± 0.46	1.24 ± 0.44	0.50
%DS	20.0 ± 7.94	19.8 ± 8.20	0.55

N= number of subjects; L= number of 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	94.3%	99.3%	<0.0001
Procedural Success	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

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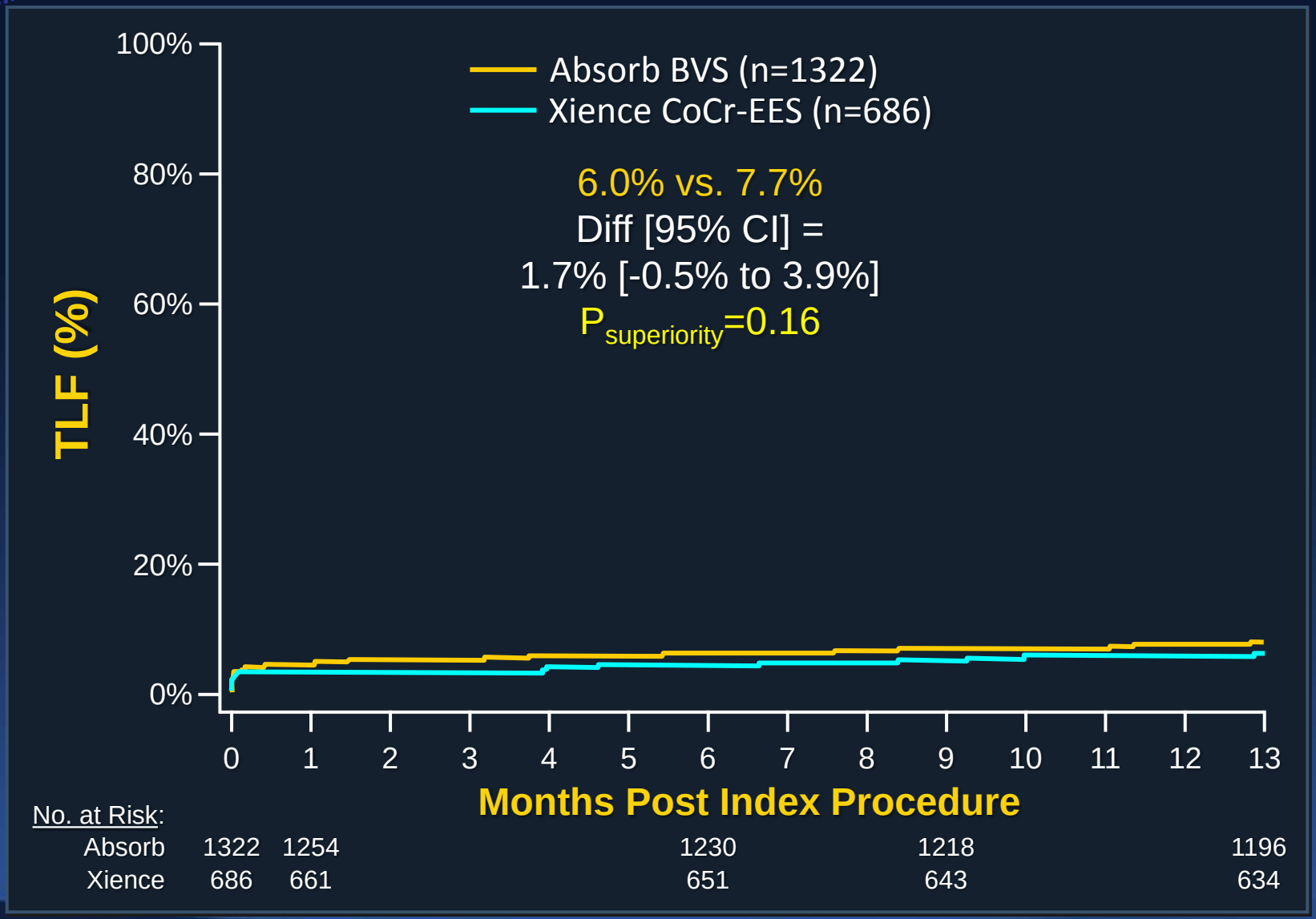
Target Lesion Failure



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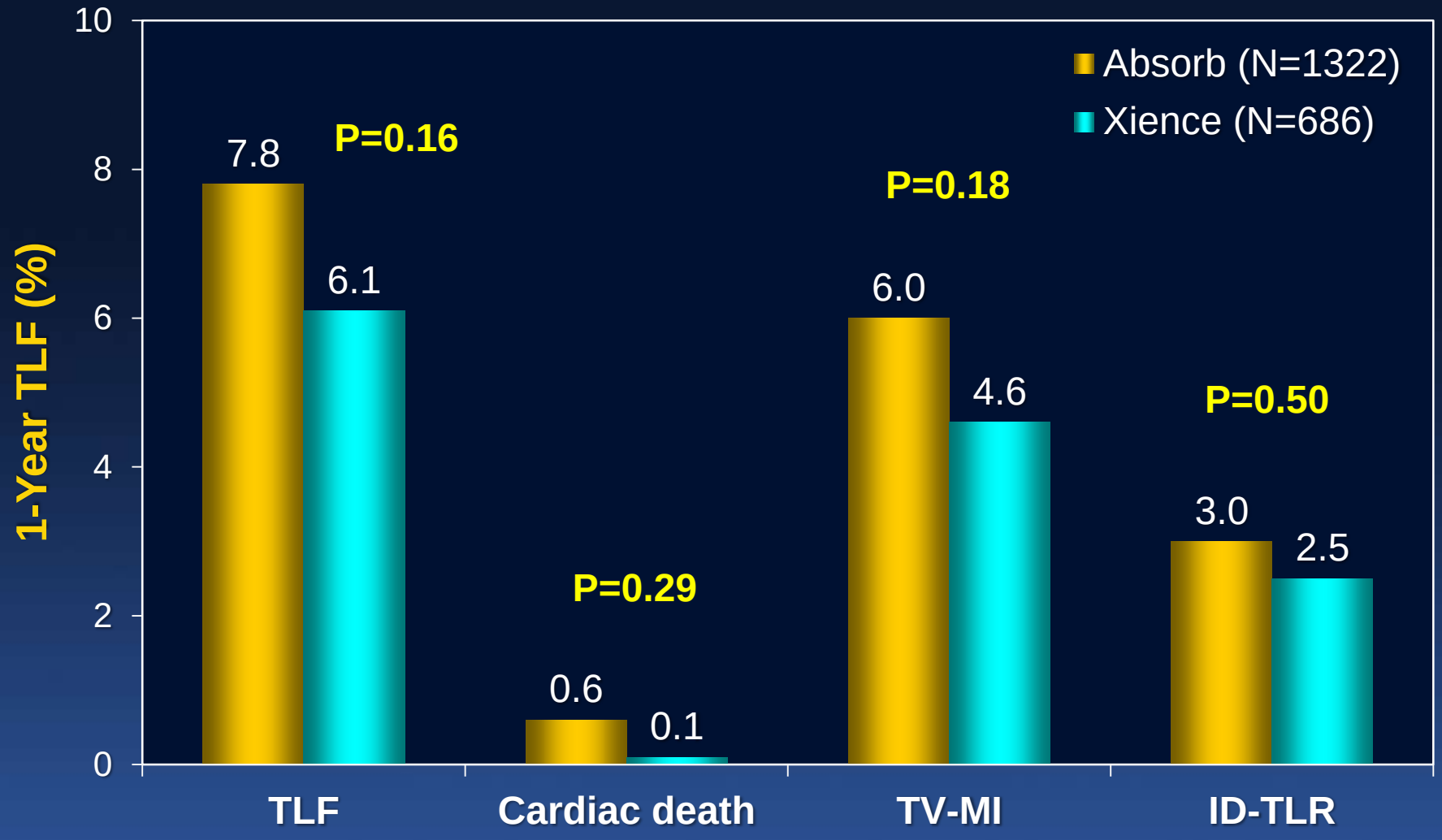
1-Year TLF: Subgroup analysis

Subgroup	Absorb (N=1322)	Xience (N=686)	RR (95% CI)	Relative Risk (95% CI)	p-value (interaction)
Age ≥64 years	8.1%	5.9%		1.37 (0.84-2.23)	0.69
Age <64 years	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 TL/TV treated	7.7%	5.8%		1.32 (0.92-1.89)	0.50
Dual TL/TV 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)	
RVD <2.63 mm	9.8%	7.8%		1.27 (0.82-1.94)	0.90
RVD ≥2.63 mm	5.7%	4.3%		1.34 (0.73-2.44)	

1-Year TLF Components



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Peri-Procedural MI by Definition

CK-MB threshold	Absorb (N=1322)	Xience (N=686)	Difference	p-value
>3x ULN	6.8%	6.6%	0.2	0.89
>5x ULN (protocol)	3.0%	2.8%	0.2	0.75
>8x ULN	1.3%	1.3%	0.0	0.96
>10x ULN	0.9%	1.2%	-0.3	0.58
SCAI definition*	0.9%	1.2%	-0.3	0.58

*>10x ULN or >5x ULN with new Q waves or new persistent LBBB
J Am Coll Cardiol 2013;62:1563-70

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

Device Thrombosis to 1 Year

	Absorb (N=1322)	Xience (N=686)	p-value
Device Thrombosis (def*/prob)	1.54%	0.74%	0.13
- Early (0 to 30 days)	1.06%	0.73%	0.46
- Late (> 30 to 1 year)	0.46%	0.00%	0.10
- Definite* (1 year)	1.38%	0.74%	0.21
- Probable (1 year)	0.15%	0.00%	0.55

*One “definite ST” in the Absorb arm by ITT was in a pt that was treated with Xience

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Powered Secondary Endpoints

	Absorb (N=1322)	Xience (N=686)	p-value
Angina	18.3%	18.4%	0.93
All Revascularization	9.1%	8.1%	0.50
ID-TVR	5.0%	3.7%	0.21

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ABSORB III Analysis In Very Small Vessels

- Additional subgroup analyses were conducted to explore the differences in device thrombosis rates between Absorb and Xience
- Given the thicker struts of Absorb, a biologically relevant analysis was to examine outcomes in very small vessels
- We therefore performed detailed analyses according to reference vessel diameter (RVD) by QCA
- Note: QCA under-estimates visually assessed vessel diameter; 2.5 mm diameter by visual assessment (smallest RVD intended for Absorb) is ~2.25 mm by QCA

Device Thrombosis by Vessel Size

Any QCA RVD <2.25 mm vs. all RVD ≥2.25 mm

Any QCA RVD <2.25 mm

1-year results Absorb vs. Xience

4.6% vs. 1.5% respectively

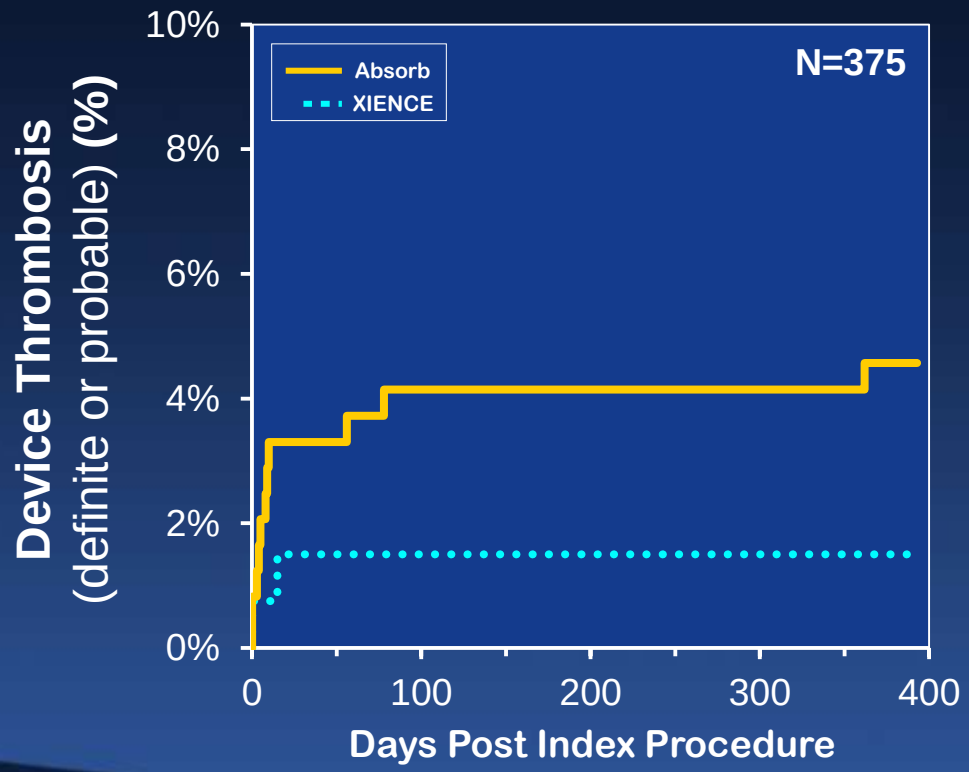
Diff [95%CI] = 3.1 [-0.3, 6.4]

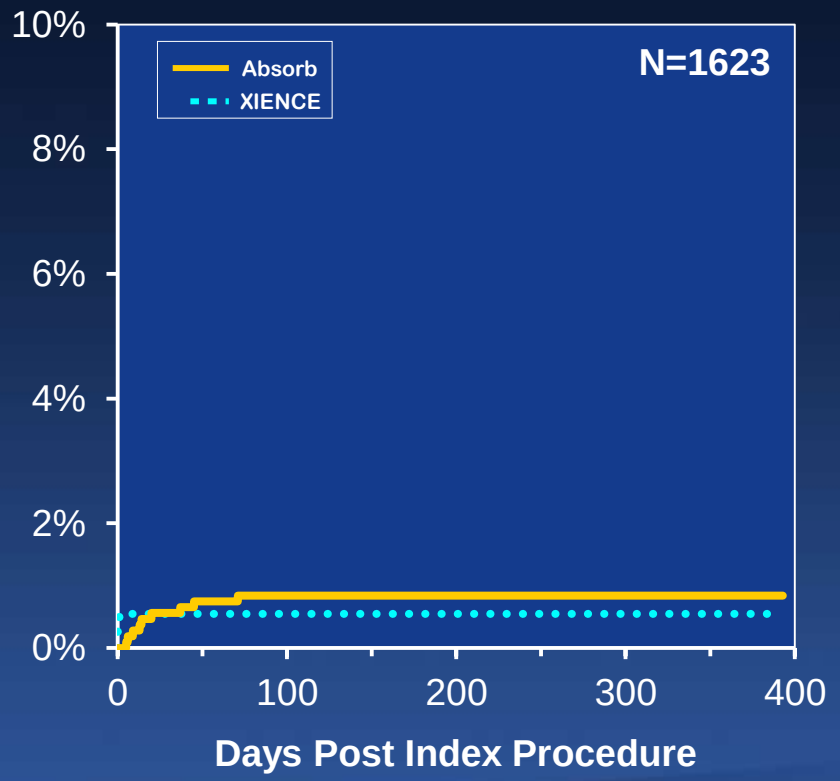
All QCA RVD ≥2.25 mm

1-year results Absorb vs. Xience

0.8% vs. 0.5% respectively

Diff [95%CI] = 0.3 [-0.5, 1.1]





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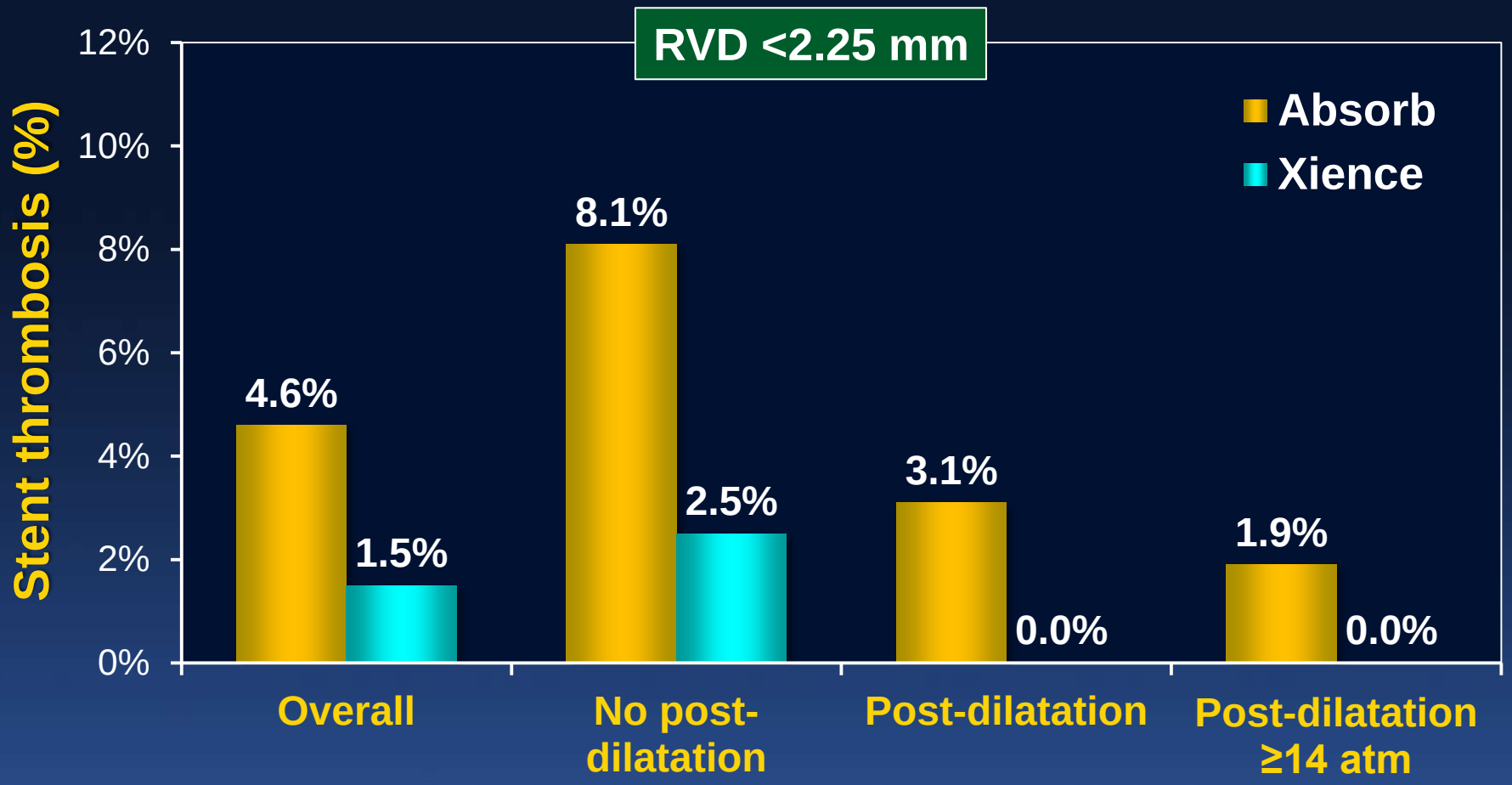
1-Year ST in Very Small Vessels

Impact of Post-Dilatation and Pressure



	Overall	No post-dilatation	Post-dilatation	Post-dilatation ≥14 atm
Absorb:	11/238	6/74	5/164	2/105
Xience:	2/133	2/79	0/54	0/36

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Summary and Conclusions (1)

- ABSORB BVS was non-inferior to Xience CoCr-EES for TLF at 1 year (primary endpoint met)
- TLF components (cardiac death, TV-MI, ID-TLR) were not significantly different between devices
- Angina, all revascularization and ID-TVR were similar between devices
- No statistically significant differences in device thrombosis were present

Summary and Conclusions (2)

- The ABSORB III trial has demonstrated safety and efficacy of Absorb BVS at 1 year in patients with stable CAD and stabilized ACS
- March 15th, 2016: FDA Advisory Board Panel voted 9-0 that Absorb was safe and effective for its intended use
- Longer term evaluation is ongoing to determine if ABSORB improves late outcomes compared to Xience

ABSORB III

Small Vessel Analysis Conclusions

- Compared to the thin strut XIENCE metallic DES, the thicker strut Absorb BVS results in similar 1-year outcomes in coronary arteries with QCA RVD ≥2.25 mm, but may have higher event rates in very small vessels
- These findings have important implications for device selection (and potentially technique) to optimize 1-year outcomes when selecting patients and lesions for Absorb BVS