Current Status and Future of BRS in U.S.

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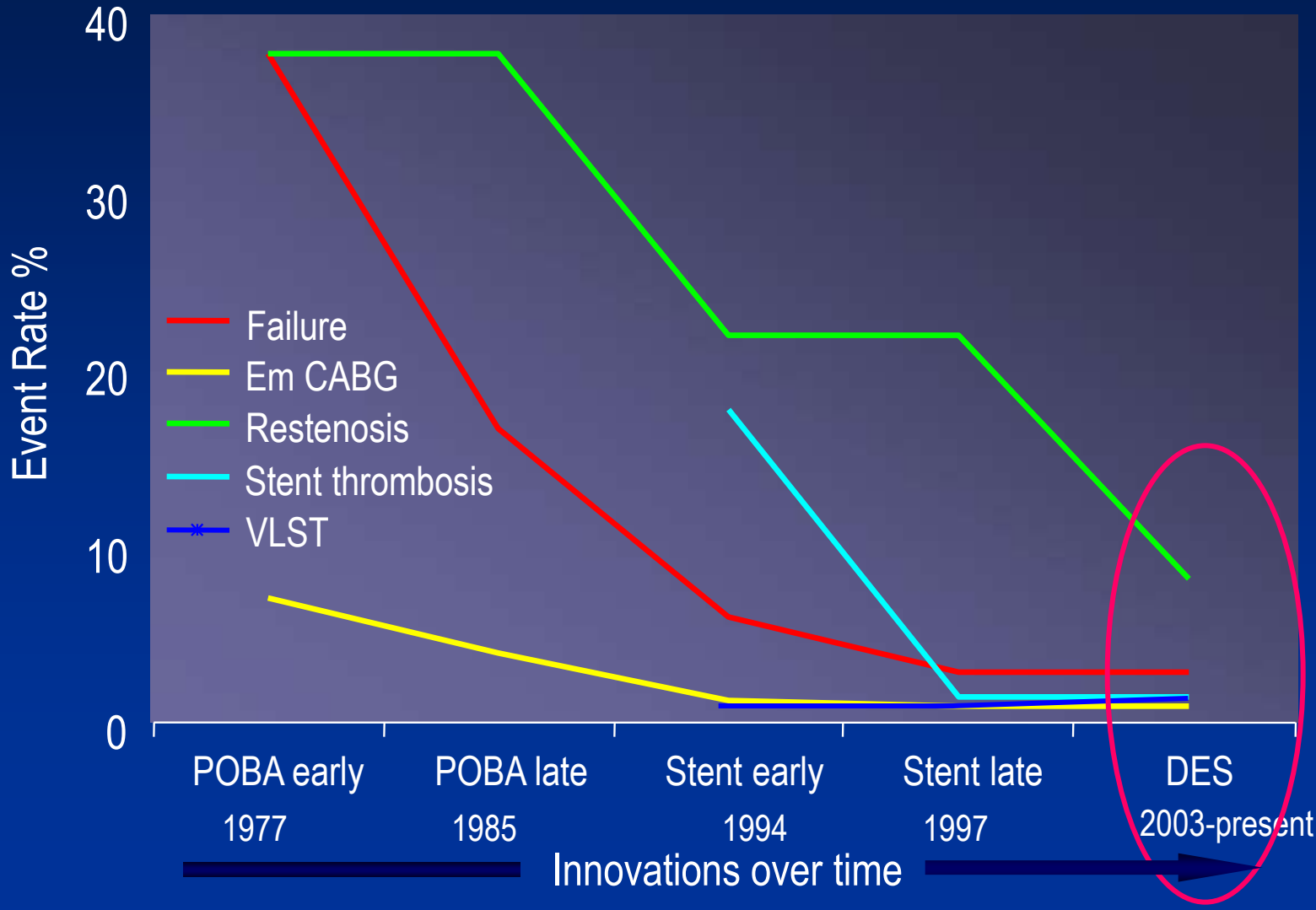
Disclosure Statement of Financial Interest

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
• Grant/Research Support	• Abbott Vascular, Medtronic
• Scientific Advisory Board	• Medtronic, Abbott Vascular
• Executive Physician Council	• Boston Scientific Corp

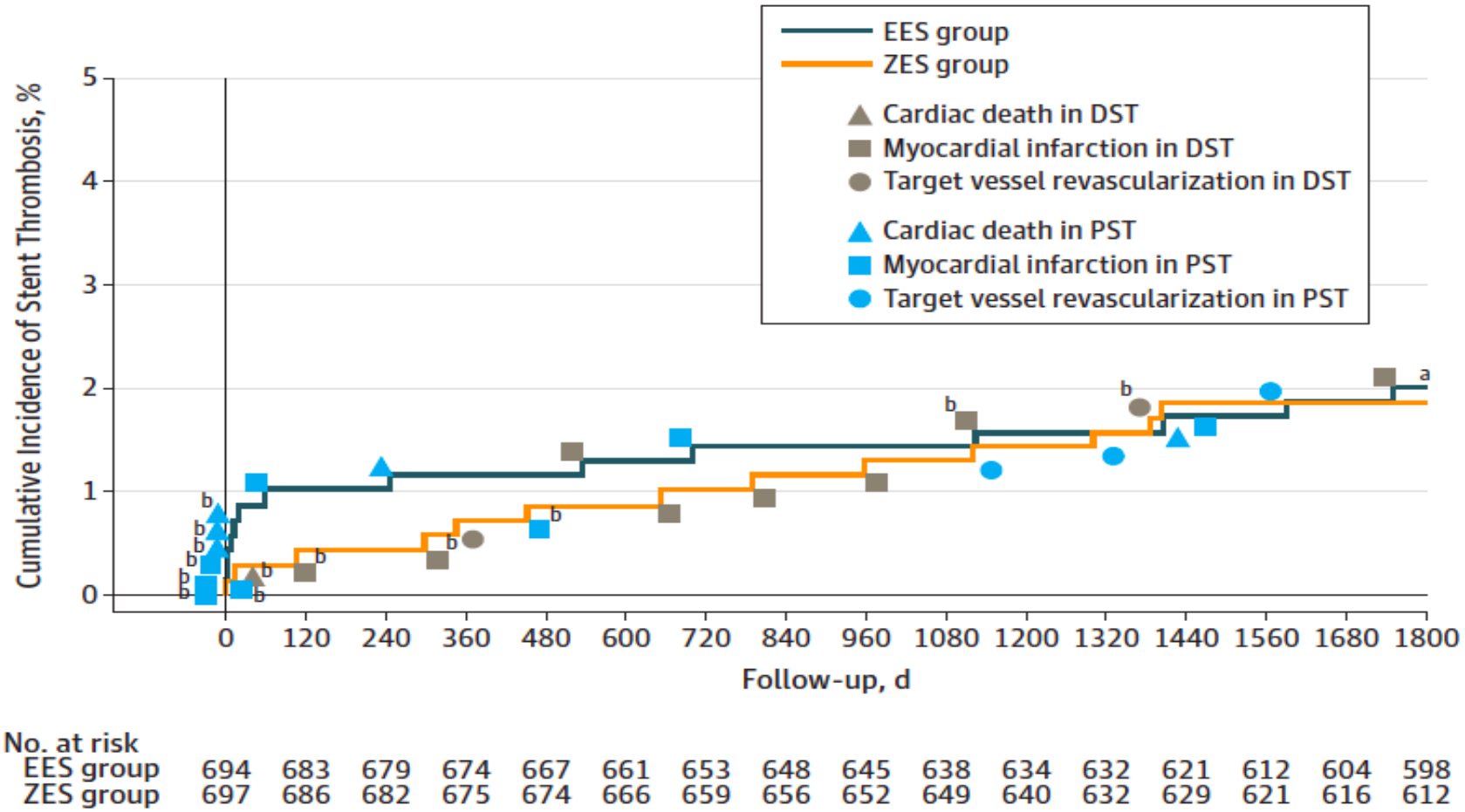
Evolution of PCI:
The Dominant Coronary Revascularization Therapy

Progressive improvements in success, safety, and durability,
as serial new technologies have been launched.



The Comparator (1) - 5-Year ST of G2 DES

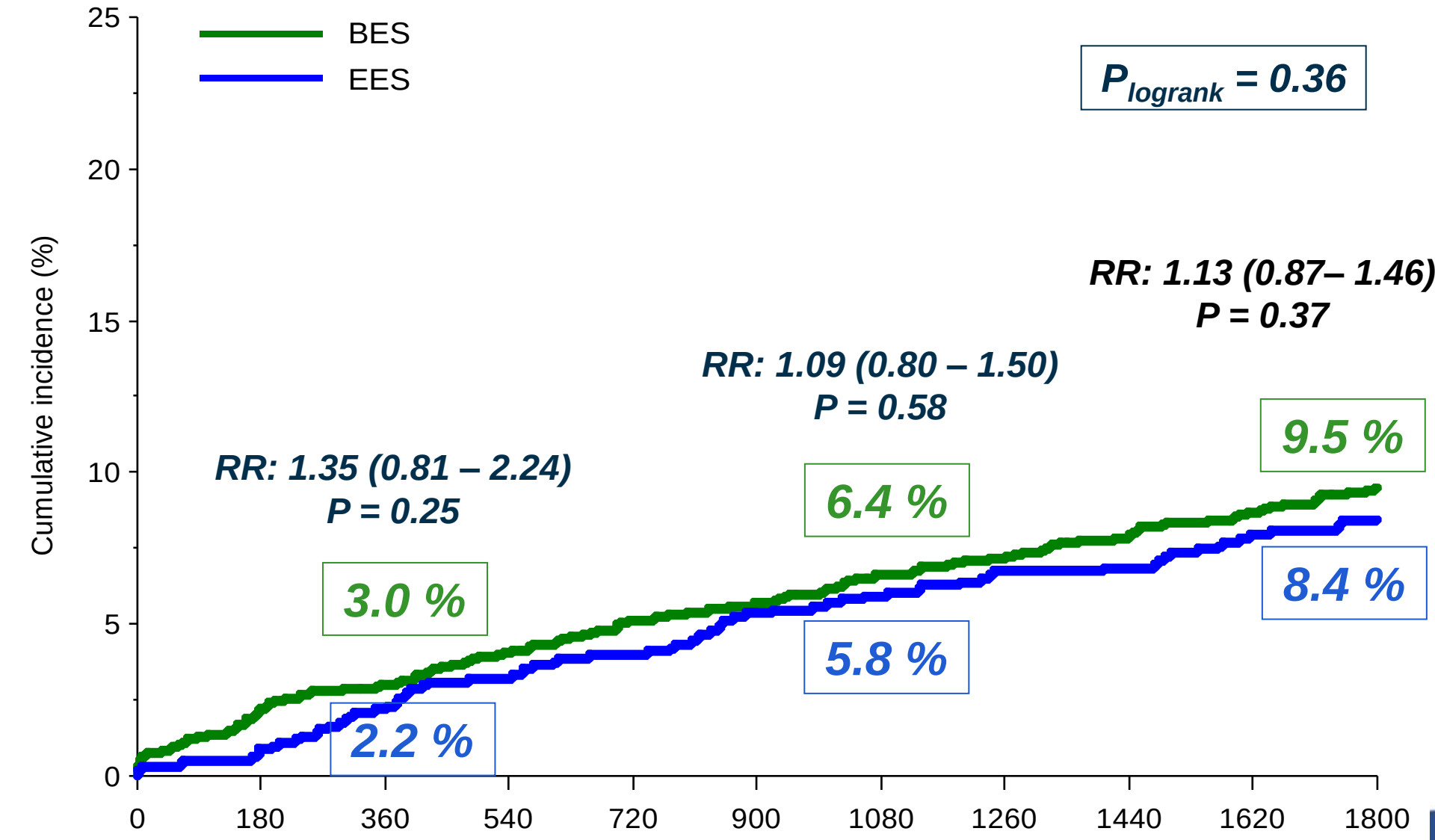
1,370 patients treated with second-generation EES or ZES from the TWENTE trial



Von Birgelen C et JAMA Cardiology 2017 [ePub ahead of print]

Compare II

CI-TVR @ 5 year



CI-TVR = Clinically Indicated Target Vessel Revascularisation

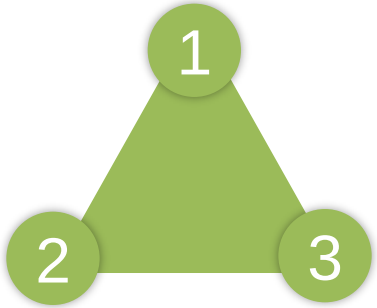
DES UNMET NEEDS

- Continue TLF creep after one year
- Side branch jailing
- Permanent presence of incomplete opposition
- Diffuse disease stenting leading to full metal jacket
- Lack of Vulnerable plaque treatment strategy
- Permanent absence of vasomotion
- Permanent implant

BRS (Absorb)

Revascularization

with Transient Support



Restoration

of Physiological Environment (shear stress, multidirectional motion, morphology)

Benign

Resorption

For Absorb, the goal is to provide temporary vessel support and then resorb, allowing for natural vessel movement and remodeling.

State of BRS (Absorb) in US

- FDA approved the Absorb GTI in 7/2016
- Calculated roll out to Absorb IV sites
- Absorb III 2 year data presented at ACC on 3/18/2017
- FDA's Letter to Health Care provider on same day 3/18/2017
  - increased MACE 11% vs 7.9%
- Absorb IV stopped enrollment at 2600 instead of 3000 with sufficient power on 3/27/2017
- AIDA in NEJM 3/29/2017
- Current Absorb penetration is << 5% and mainly in 10 cath labs of early adopters/true believers.
- Concern for litigation (risk vs benefits)

How did we get here ?

Revascularization

Comparative Function of BVS and EES

ABSORB II - 501 patients randomized 2:1 to Absorb or Xience

	Absorb	Xience	P value
MLD (mm)			
Pre-procedure	1.06 ± 0.33	1.06 ± 0.31	0.81
Post-procedure	2.22 ± 0.33	2.50 ± 0.33	<0.0001
Acute gain	1.16 ± 0.38	1.45 ± 0.37	<0.0001
3-Year follow-up	1.86 ± 0.54	2.25 ± 0.37	<0.0001
Net gain	0.80 ± 0.61	1.20 ± 0.44	<0.0001
Late loss*	0.37 ± 0.45	0.25 ± 0.25	0.0003
Binary restenosis (%)	7.0%	0.7%	0.0031

*Co-primary endpoint. MLD = minimal lumen diameter

Serruys PW, et al. Lancet. 2016;388:2479-2491

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

Acute Success

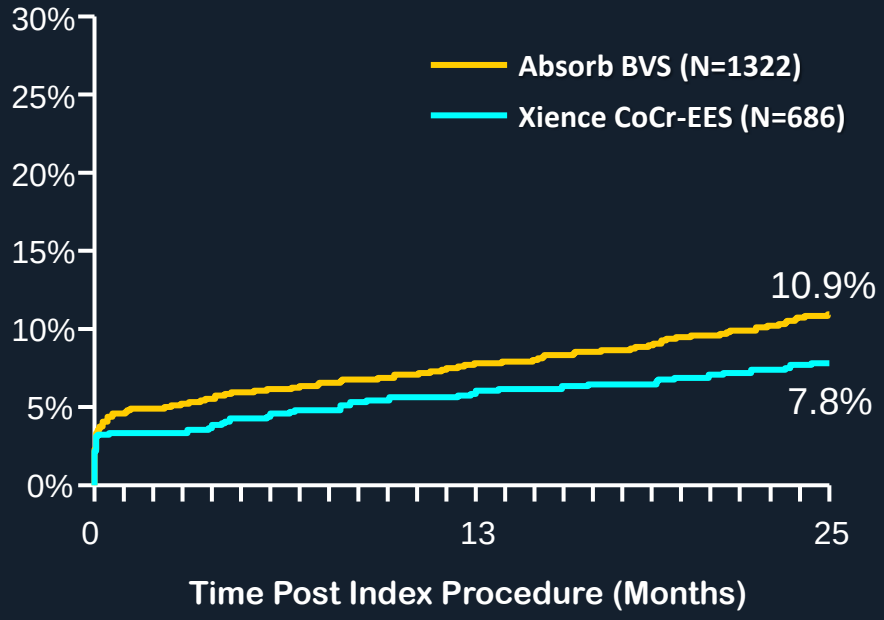
	Absorb (N=1322) (L=1385)	Xience (N=686) (L=713)	p-value
Device Success	94.3%	99.3%	<0.0001
Procedural Success	94.6%	96.2%	0.12

- **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

TLF by 2 Years (25 Months)

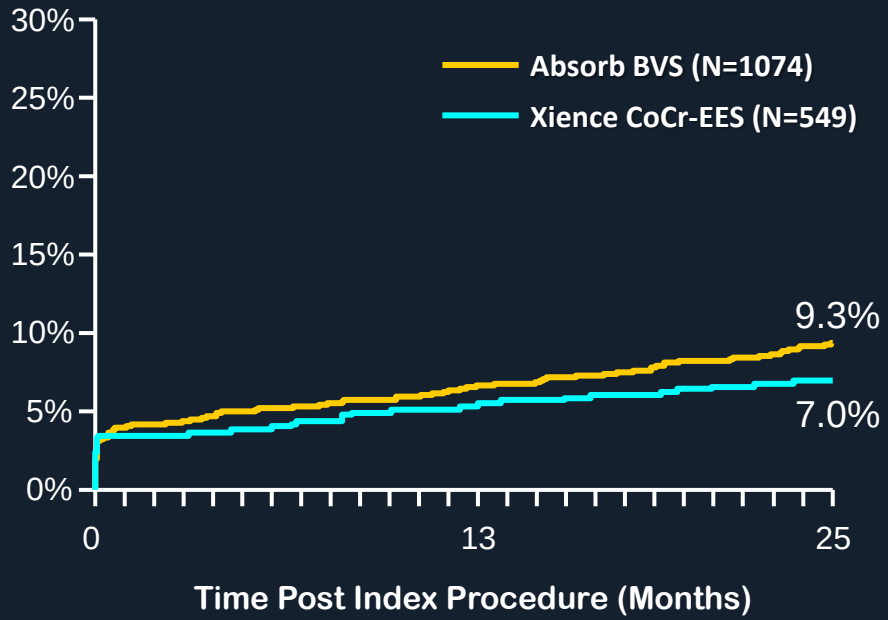
Overall

HR [95%CI]=1.42 [1.04, 1.94]
p=0.03



QCA RVD ≥ 2.25 mm

HR [95%CI]=1.35 [0.93, 1.96]
p=0.12



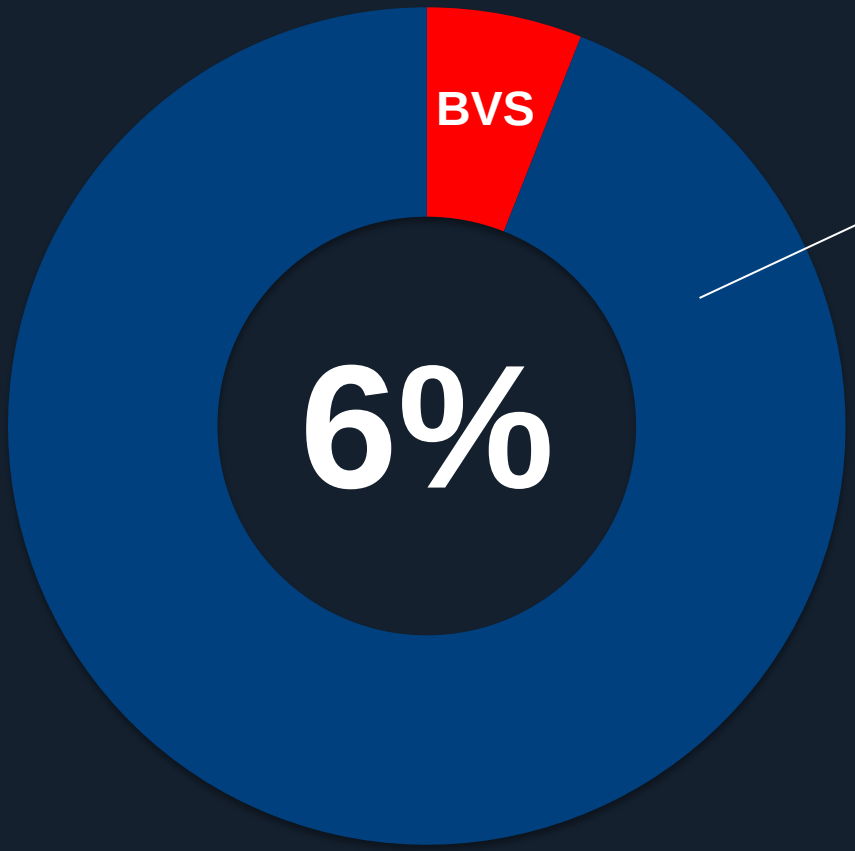
No. at Risk:

Absorb	1322	1193	1141	1074	982	943
Xience	686	634	608	549	512	496

Note: The 2-year window allowed follow-up through 25 months

Bioresorbable Scaffolds: Why Not?

573 consecutive patients (741 lesions) by 24 operators at 5 sites (Sep 2016 - Jan 2017)



Interim analysis (57% of planned sample size)

Did not implant a BVS, because…*	
Calcifications	31%
Small vessel	23%
Bifurcation	15%
STEMI	14%
ISR	13%
Long Lesion/Multiple Overlap	13%
Large Vessel	13%
Tortuous/angulated vessel	11%
Elderly	9%
Time issues	8%
Ostial Lesions	7%

*Muliple answers allowed

ABSORB-SELECT Study Investigators

The Scaffold, the Lesion or the Doctor?

P

Prepare the vessel to be re-engineered

Pre-dilate using a 1:1 balloon-to-artery ratio using a non-compliant balloon (it can also help accurately size the vessel). Use plaque-modification devices if needed. Confirm full expansion of balloon and residual stenosis of 20-40% in 2 orthogonal views.

S

Size the vessel appropriately

Select the scaffold size for the best fit. Consider using intravascular ultrasound (IVUS), optical coherence tomography (OCT) or quantitative coronary angiography (QCA) to aid vessel sizing. **Note:** Absorb BVS is indicated for vessels with a reference vessel diameter of ≥ 2.5 mm and ≤ 3.75 mm.

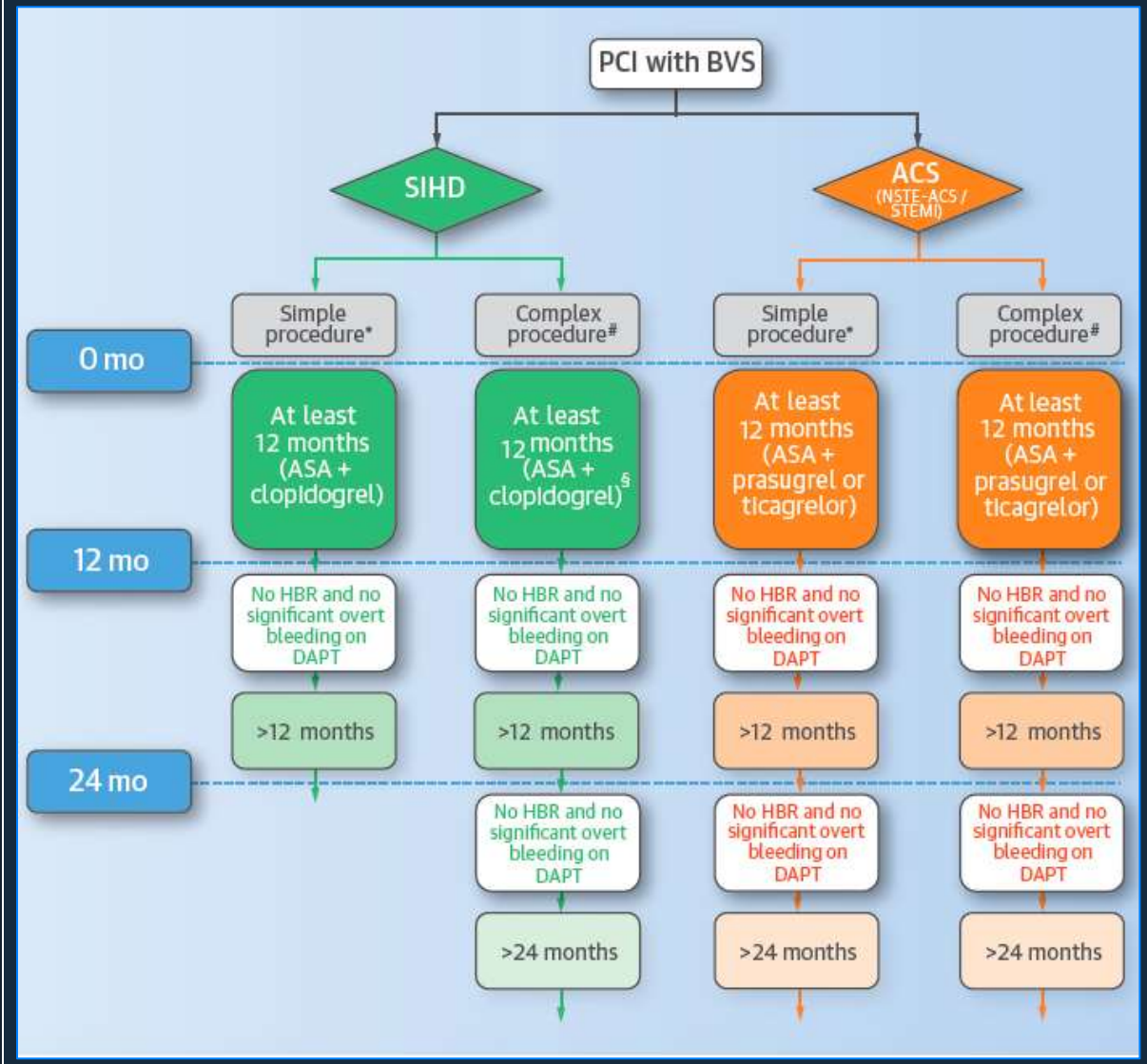
P

Post-dilate to embed the struts into the vessel wall

Dilate to high pressure with a non-compliant balloon up to 0.5 mm above nominal scaffold diameter. Verify <10% final residual stenosis in 2 orthogonal views, and ensure full strut apposition.

Abbott Vascular

DAPT duration After BVS Implantation



* Simple procedures include 1 BVS implanted in ACC/AHA A/B_1 lesions.

Complex procedures include 1 BVS implanted in ACC/AHA B_2/C lesions, >1 BVS implanted on lesions of any ACC/AHA type, or any other unfavorable clinical, angiographic and procedural characteristics.

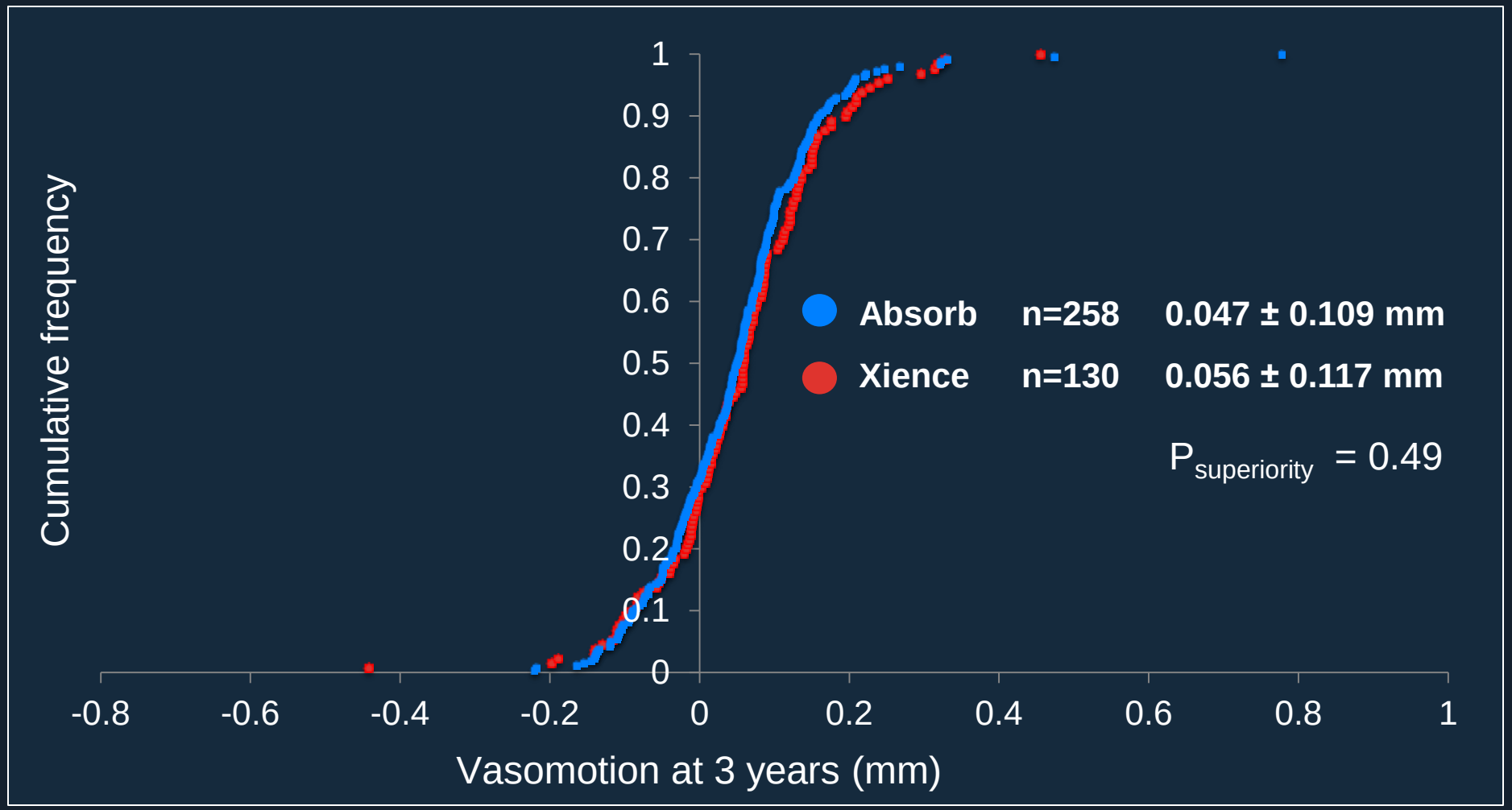
§ Considerations on the use of aspirin in combination with prasugrel or ticagrelor for the initial 30 days, followed by switch to aspirin and clopidogrel, may prevail based on the individual risks of ischemia and bleeding.

Capodanno D, Angiolillo DJ. JACC: Cardiovasc Interv 2017 [In press]

Restoration

Comparative Vasomotion of BVS and EES

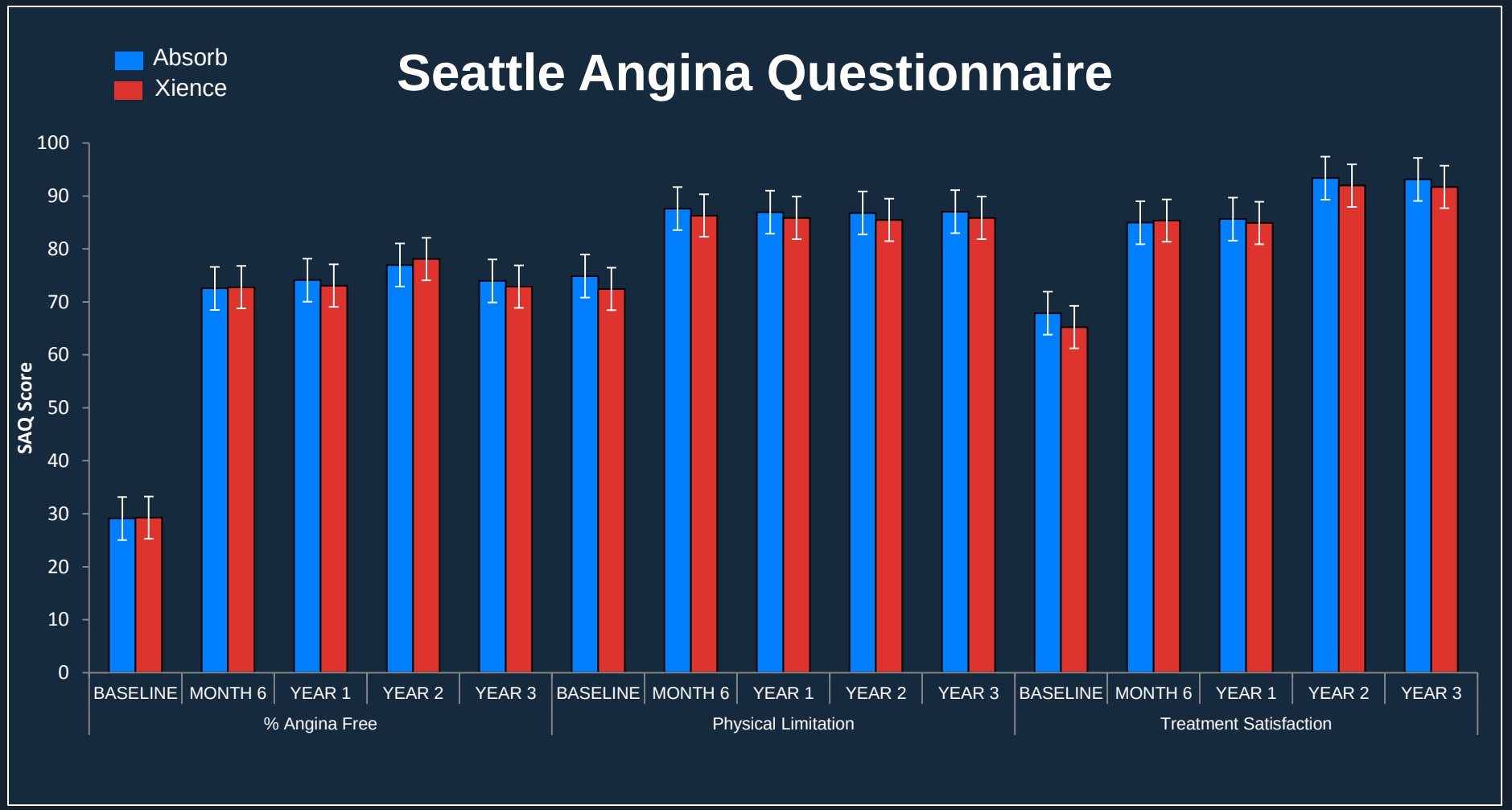
ABSORB II - 501 patients randomized 2:1 to Absorb or Xience



Serruys PW, et al. Lancet. 2016;388:2479-2491

Comparative Angina of BVS and EES

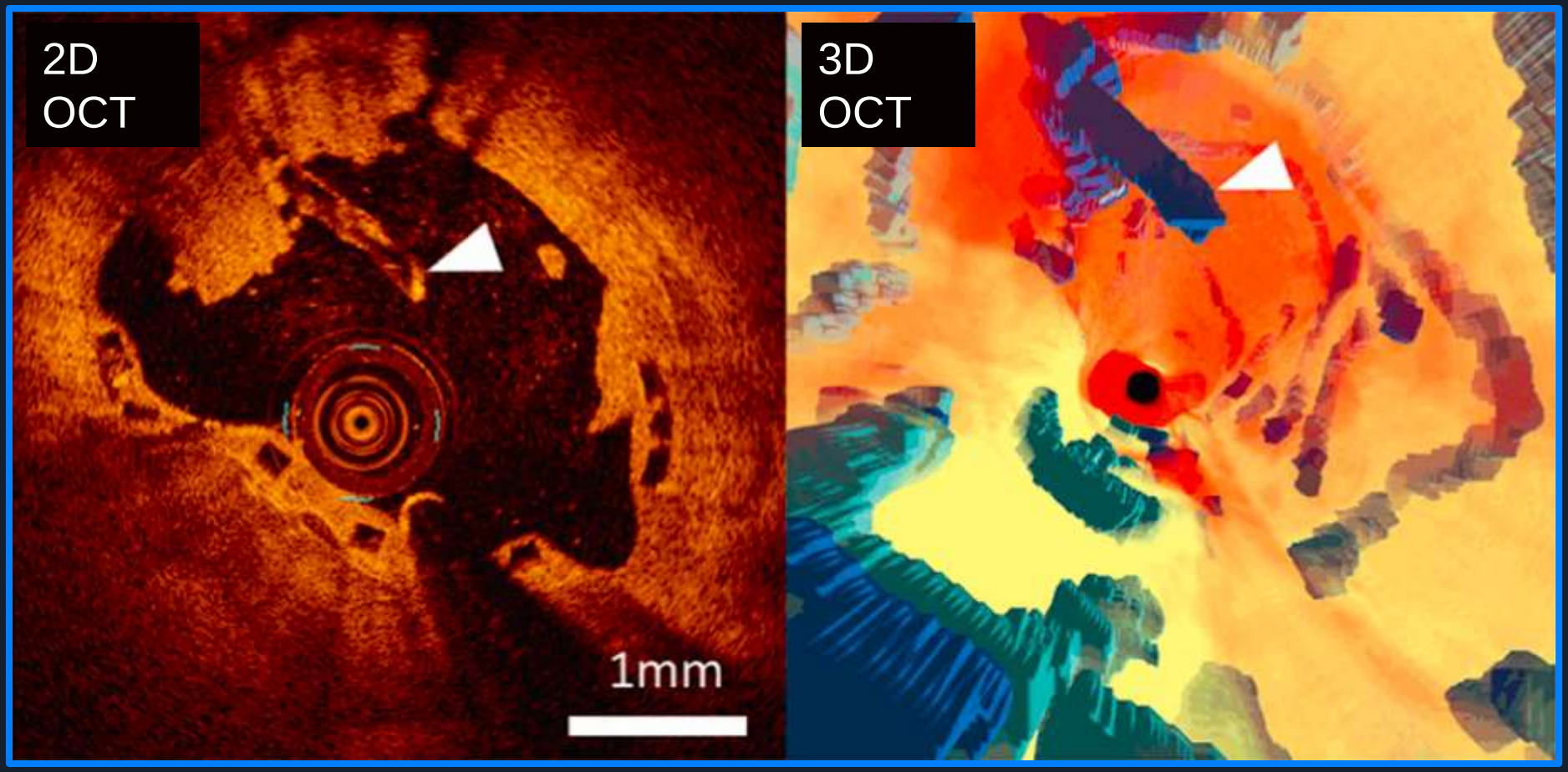
ABSORB II - 501 patients randomized 2:1 to Absorb or Xience



Serruys PW, et al. Lancet. 2016;388:2479-2491

Resorption (Benign ?)

Intraluminal Scaffold Dismantling
A BRS-specific Thrombosis Mechanism



Strut discontinuity with marked suppression of neointimal hyperplasia resulting in prolapse of a scaffold segment into the vessel lumen before absorption is complete

Raber L, et al. J Am Coll Cardiol. 2015;66:1901-14

Very Late Scaffold Thrombosis

ABSORB II - 501 patients randomized 2:1 to Absorb or Xience

	Absorb	Xience	P value
Definite	**2.5%**	**0.0%**	**0.06**
Acute	0.3%	0.0%	1.00
Subacute	0.3%	0.0%	1.00
Late	0.0%	0.0%	1.00
Very late	1.8%	0.0%	0.19
Definite or probable	**2.8%**	**0.0%**	**0.03**
Acute	0.3%	0.0%	1.00
Subacute	0.3%	0.0%	1.00
Late	0.3%	0.0%	1.00
Very late	1.8%	0.0%	0.19

Serruys PW, et al. Lancet. 2016;388:2479-2491

Clinical Endpoints by 2 Years (25 Months)

	Overall		QCA RVD ≥ 2.25mm	
	Absorb (N=1322)	XIENCE (N=686)	Absorb (N=1074)	XIENCE (N=549)
TLF	11.0% (143)*	7.9% (53)*	9.4% (99)	7.0% (38)
Cardiac Death	1.1% (14)	0.6% (4)	0.9% (10)	0.4% (2)
TV-MI	7.3% (95)**	4.9% (33)**	6.5% (68)	4.8% (26)
ID-TLR	5.3% (69)	4.3% (29)	4.1% (43)	3.0% (16)
ST (Def/Prob)	1.9% (24)	0.8% (5)	1.3% (13)	0.6% (3)

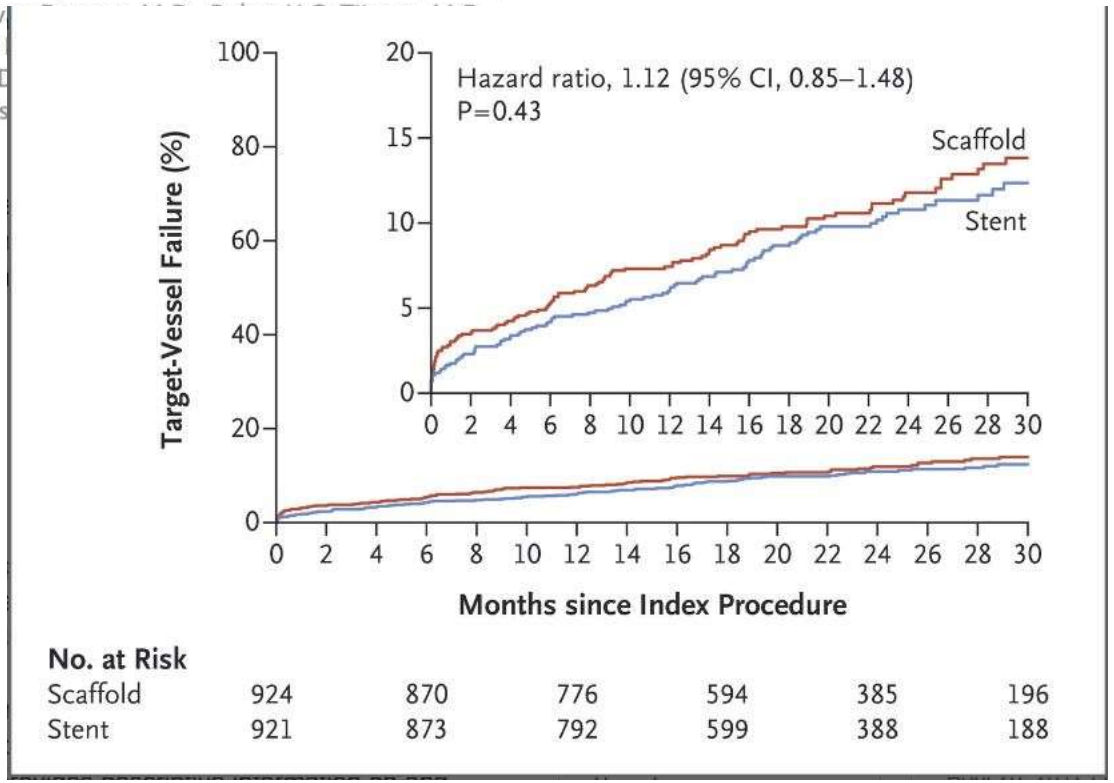
* P-value=0.03. ** P-value=0.04. P-value >0.05 for all other comparisons
Note: The 2-year window allowed follow-up through 25 months

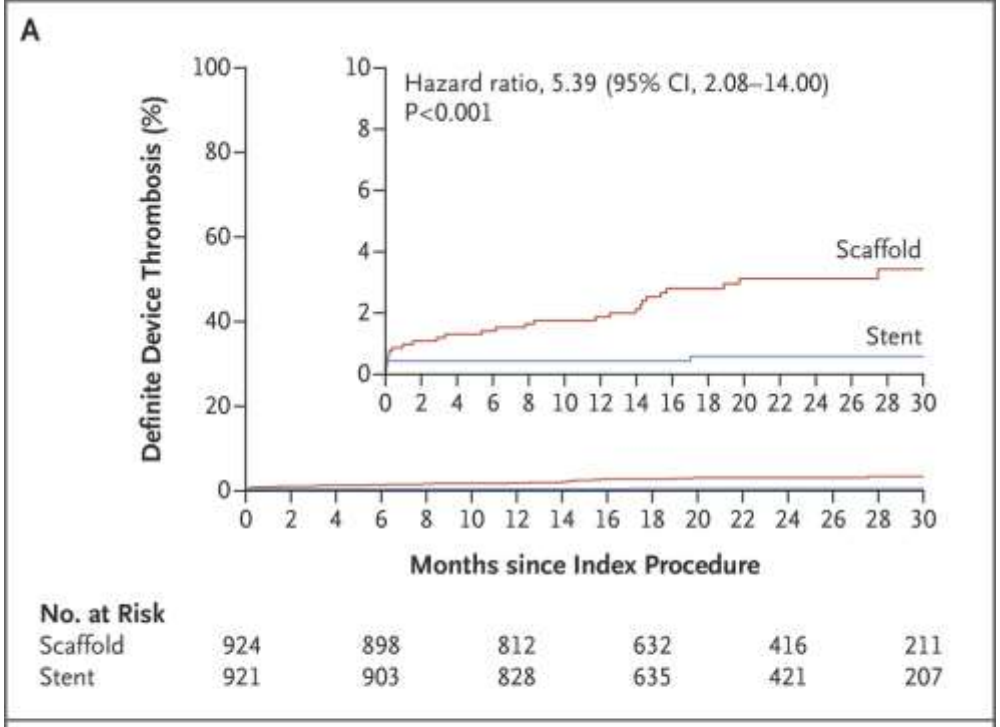
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Bioresorbable Scaffolds versus Metallic Stents in Routine PCI

Joanna J. Wykrzykowska, M.D., Ph.D., Robin P. Kraak, M.D.,
Sjoerd H. Hofma, M.D., Ph.D., Rene J. van der Schaaf, M.D., Ph.D.,
E. Karin Arkenbout, M.D., Ph.D., Alexander J. IJsselmuiden, M.D., Ph.D.,
Joëlle Elias, M.D., Ivo M. v
Karel T. Koch, M.D., Ph.D., Jan
Robbert J. de Winter, M.D., Ph.D
and Jose P.S. Henriques




A
Definite Device Thrombosis (%)
Hazard ratio, 5.39 (95% CI, 2.08–14.00)
P<0.001
Scaffold
Stent
Months since Index Procedure
No. at Risk
Scaffold 924 898 812 632 416 211
Stent 921 903 828 635 421 207
B
Definite or Probable Device Thrombosis (%)
Hazard ratio, 3.87 (95% CI, 1.78–8.42)
P<0.001
Scaffold
Stent
Months since Index Procedure
No. at Risk
Scaffold 924 898 812 632 416 211
Stent 921 903 828 634 421 207

State of BRS (Absorb) in US

Longer procedure, higher short term risk plus long term uncertainty….no clear benefits in sight!

Mitigate Risk of BRS

- Will PSP fix the early, late ST?

Blinded, Pooled, Interim ABSORB IV Outcomes: Comparison to ABSORB III

ABSORB III: 2008 pts randomized 2:1 BVS:EES (1322:686)
ABSORB IV: 3000 pts being randomized 1:1 BVS:EES

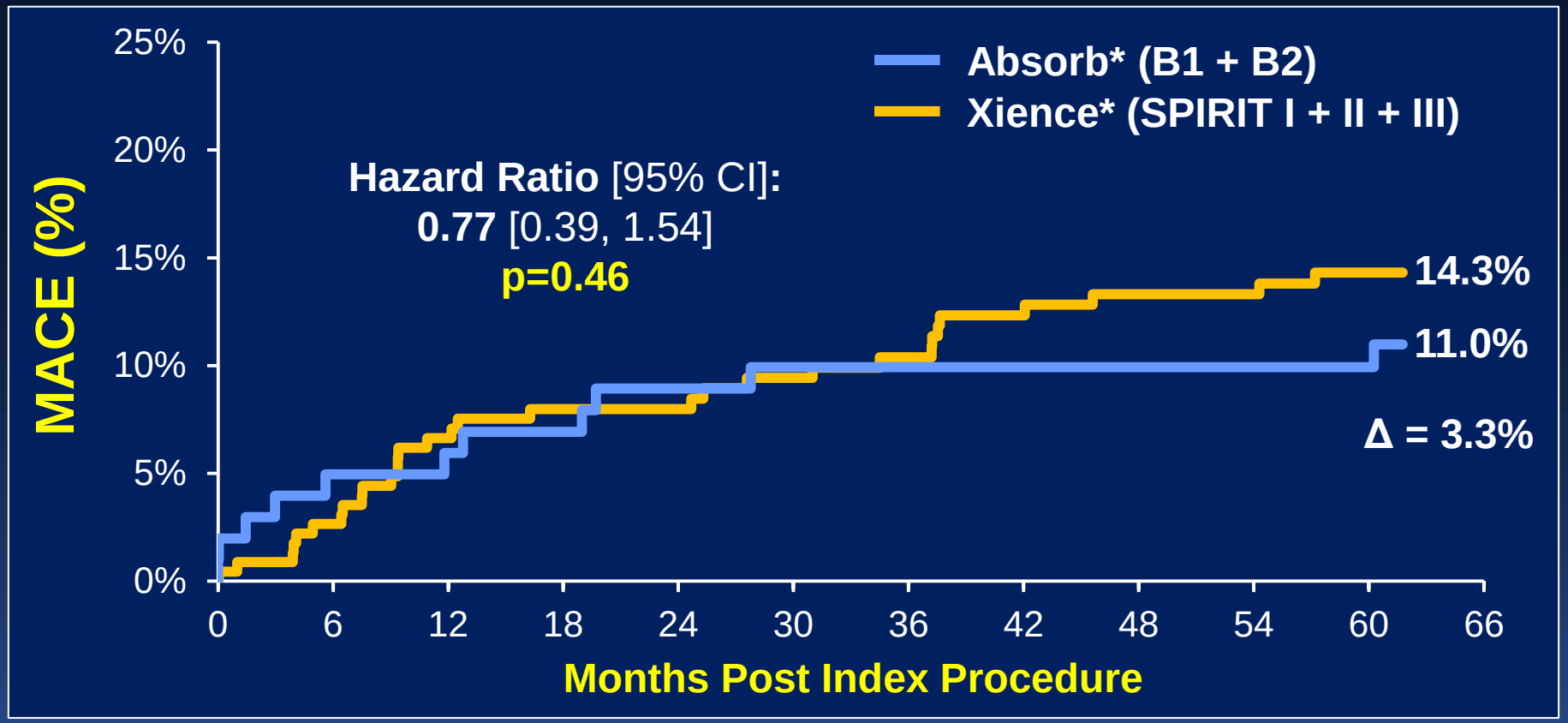
	ABSORB III Pooled (N=2008)	ABSORB III Pooled (N=2008)[1]	ABSORB IV Pooled (N=2494)[2,3]
QCA RVD <2.25 mm	19%	19%	4%
Post-dilatation (BVS)	66%	66%	83%
	Pooled stent/scaffold thrombosis		
30 days	1.0%	0.9%	0.3%
1 year	1.3%	1.1%	0.5%

1. Assuming the same event rate for each arm in ABSORB III, but with a 1:1 randomization ratio.
2. Based on January 16, 2016 data cut (N=2349 with 30 day FU and N=1297 with 1 year FU).
3. A-IV includes 25% non A-III like subjects (troponin+ NSTEMI/STEMI, 3 lesions treated, and planned staged procedures).

Future of BRS in the US

- Will PSP solve the VLST and TLF issues?
- Is resorption from year 2 to 5 a benign process in human?
- Does resorption result in a larger “golden tube” which impacts protection against neoatherosclerosis/garden variety atherosclerosis?
- Can we provide patient level benefits?

Absorb Beyond 2 Years:
Cohort B. vs Xience 5-Year FU (3.0 x 18 mm)



Days:	0	37	194	284	393	573	758	1123	1488	1853
Absorb:	101	99	96	96	94	92	91	88	86	85
Xience:	227	224	219	211	204	202	191	182	174	169

Serruys PW. TCT 2015

Compare II

POCE & DOCE (TLF)