Bioresorbable Scaffolds in a “Nutshell”: Updates and Expectations

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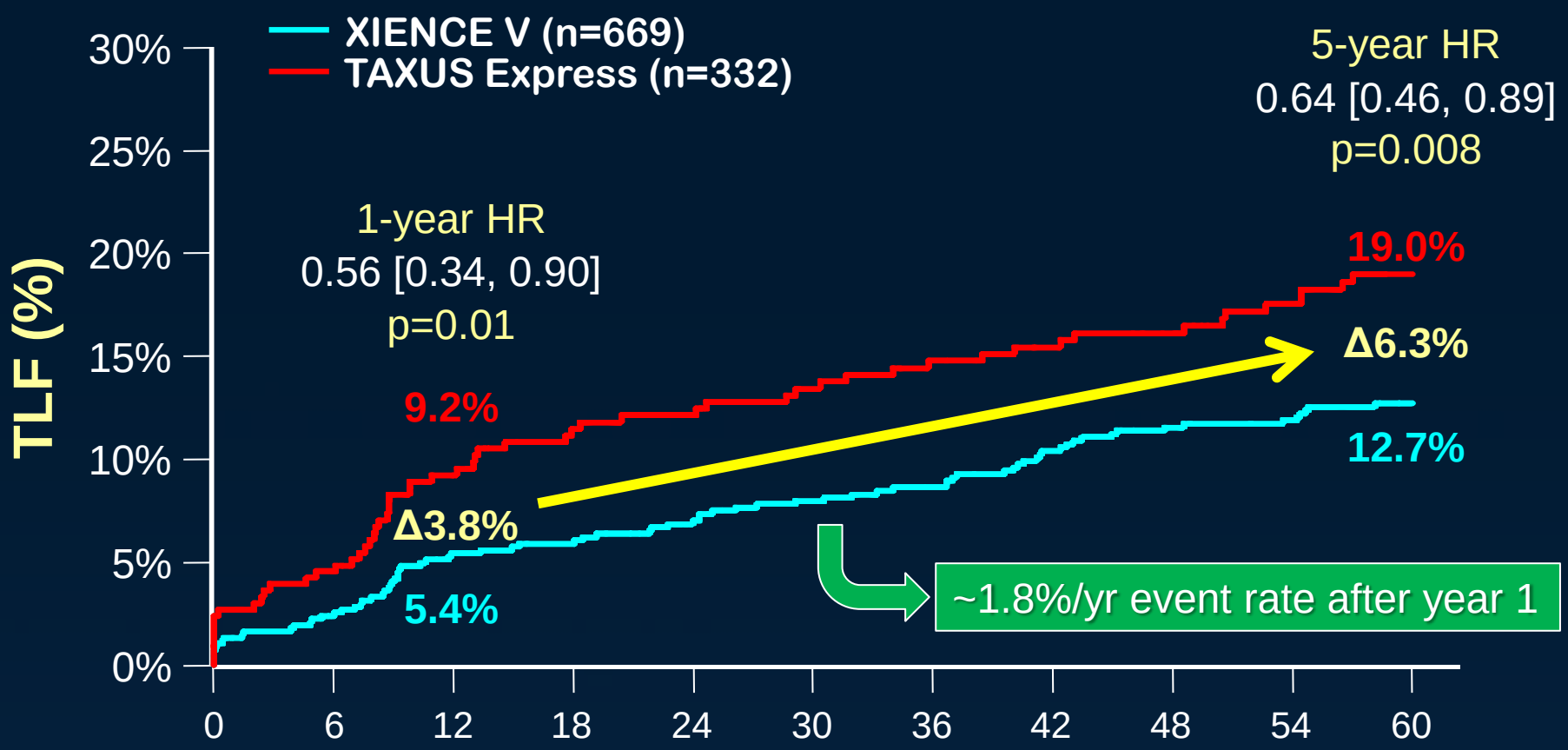
Disclosure Statement of Financial Interest

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
• Consultant	• Reva

SPIRIT III: Target Lesion Failure @5 years



Number at risk

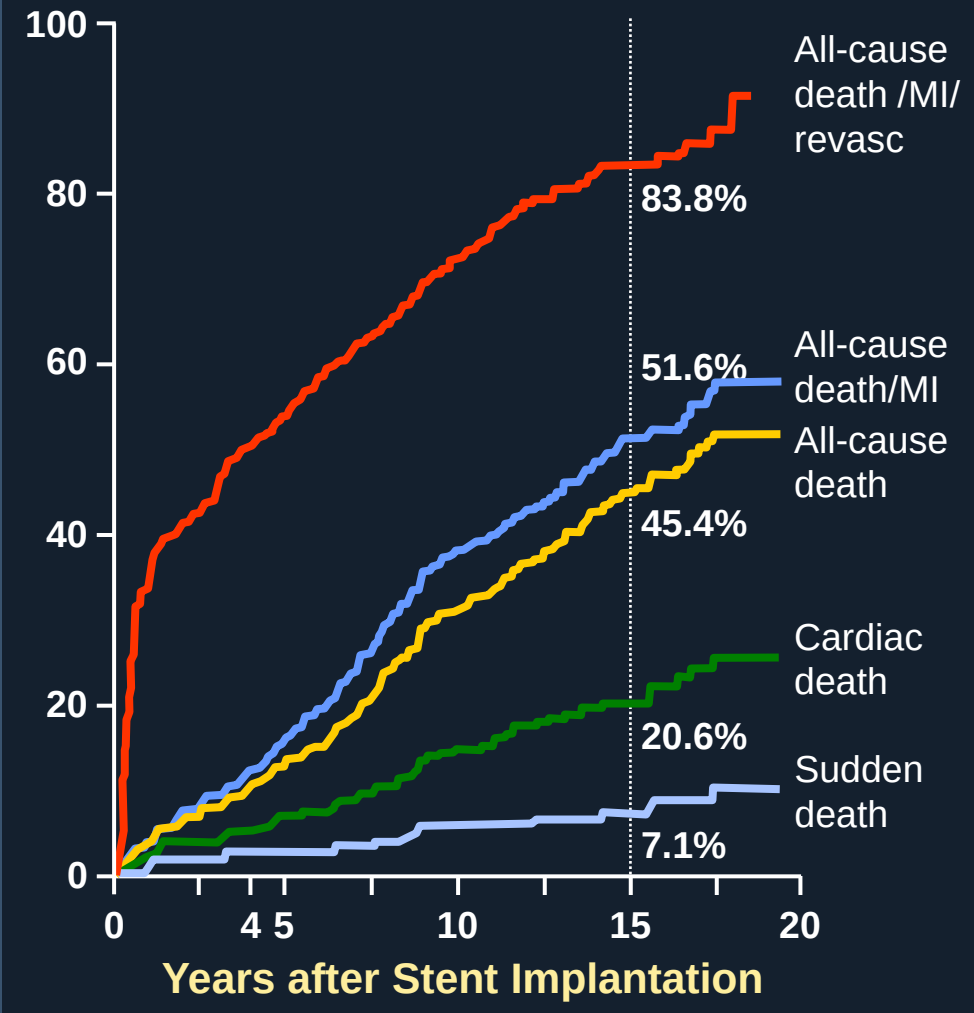
XIENCE V	669	646	616	601	582	571	565	548	537	529	521
TAXUS	332	310	288	274	269	262	255	248	243	231	223

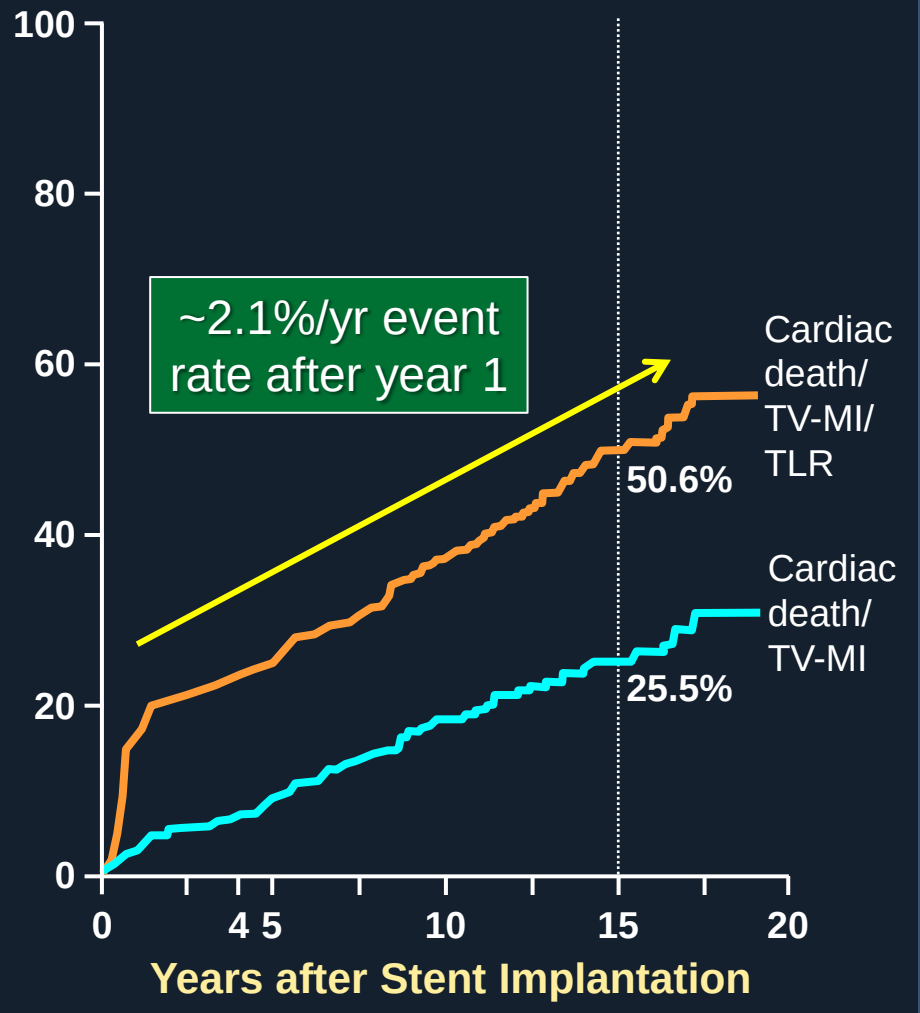
TLF = cardiac death, target vessel MI, or ischemic-driven TLR

Gada H et al. J Am Coll Cardiol Intv 2013;6:1263–6.

15-year Follow-up After BMS (1990-1993)

N=405





Yamaji K et al. *Circ CV Int* 2010

Bioresorbable Vascular Scaffolds (BRS)

Igaki-Tamai

PLLA

Abbott Absorb

PLLA
(eluting everolimus)

Elixir DESolve

PLLA
(eluting novolimus)

Reva ReSolve

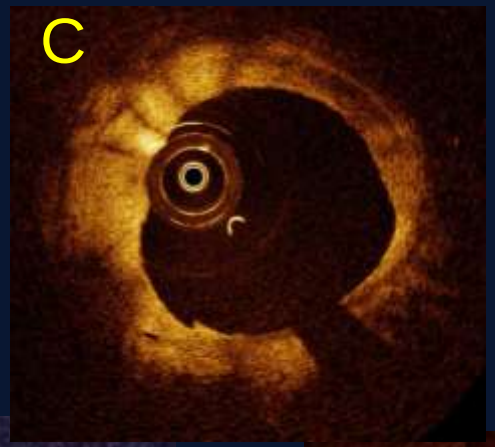
Iodinated tyrosine-derivative
(eluting sirolimus)

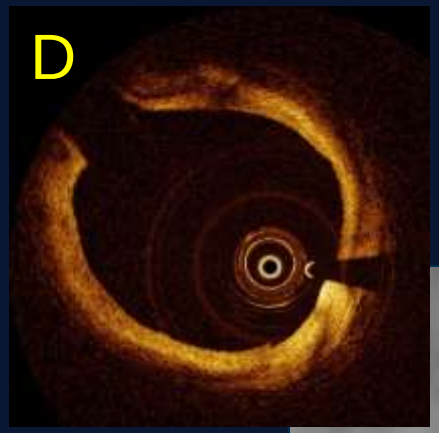
Biotronik Dreams

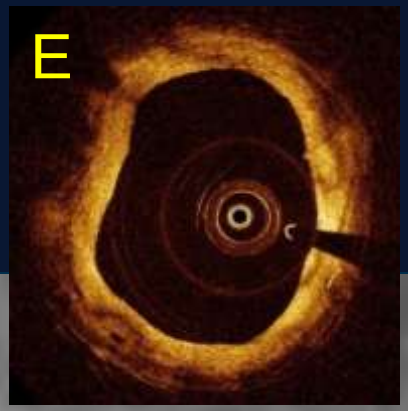
Magnesium
(eluting sirolimus)

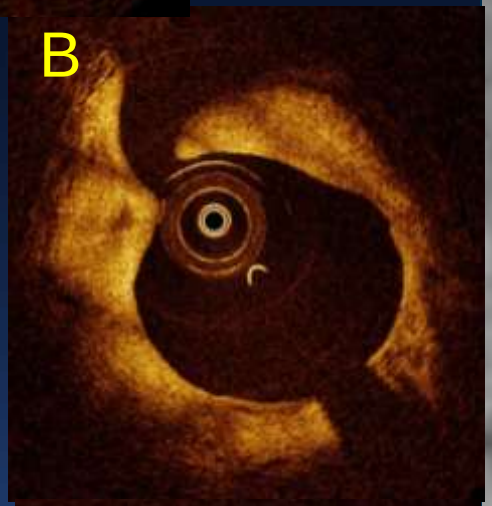
Igaki-Tamai stent at 10 years!

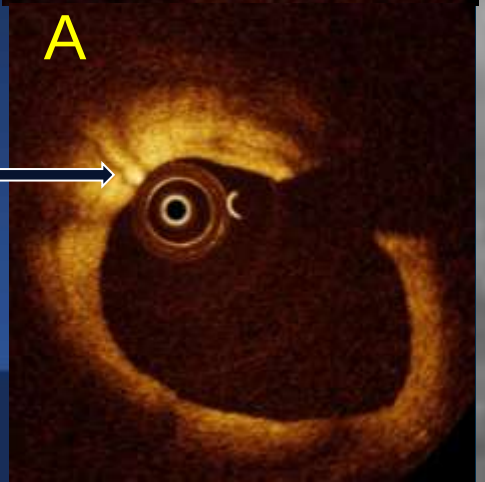
Gold markers *

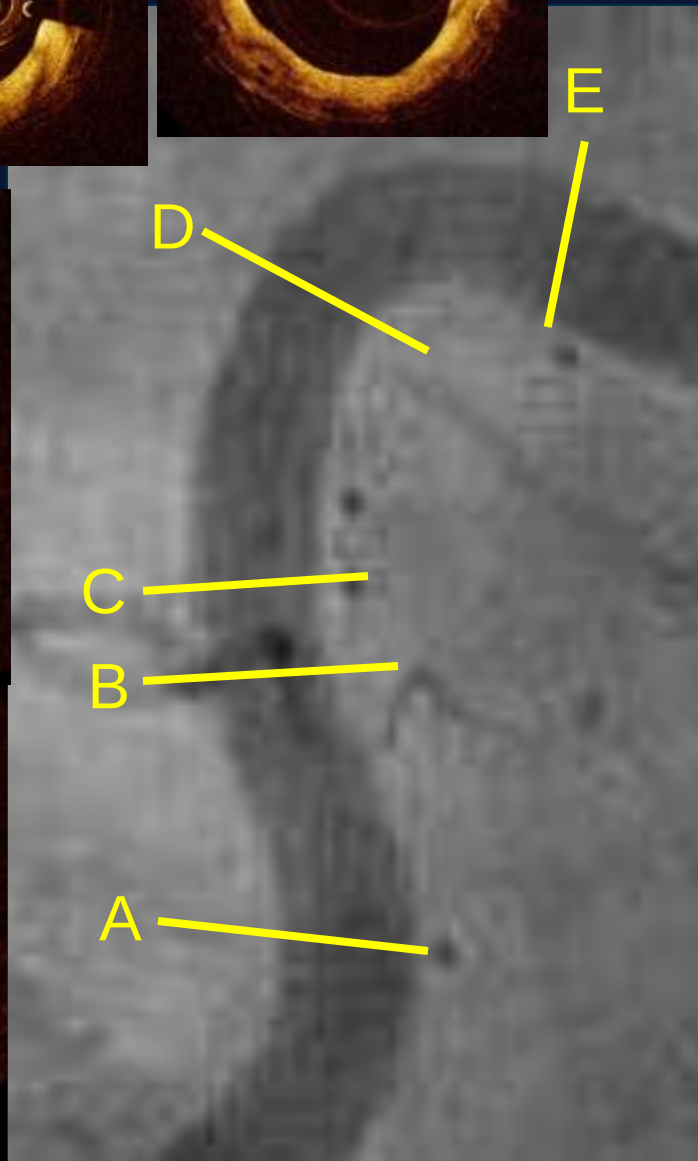










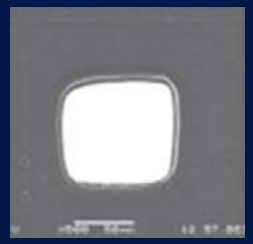
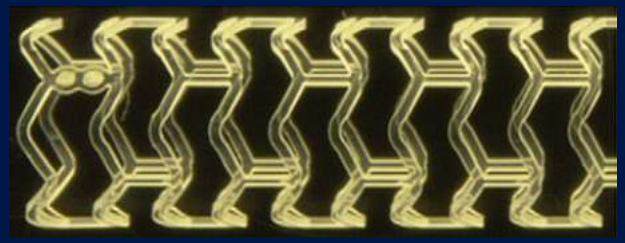
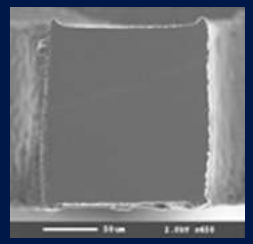


Onuma Y et al. EuroInt 2009

Opportunities for BRS

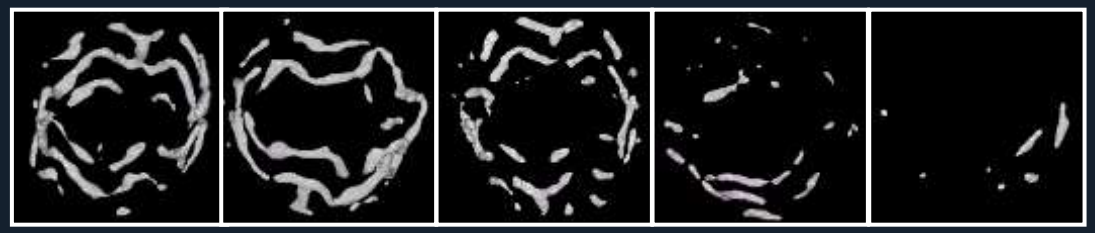
- Workhorse lesions
- Specific patient and lesion subsets
  1. Young patient
  2. Diabetic
  3. Bifurcations and LM (unjailing)
  4. Diffuse disease and full metal jacket
  5. Chronic total occlusions
  6. In-stent restenosis
  7. Acute coronary syndromes
  8. Vulnerable plaque

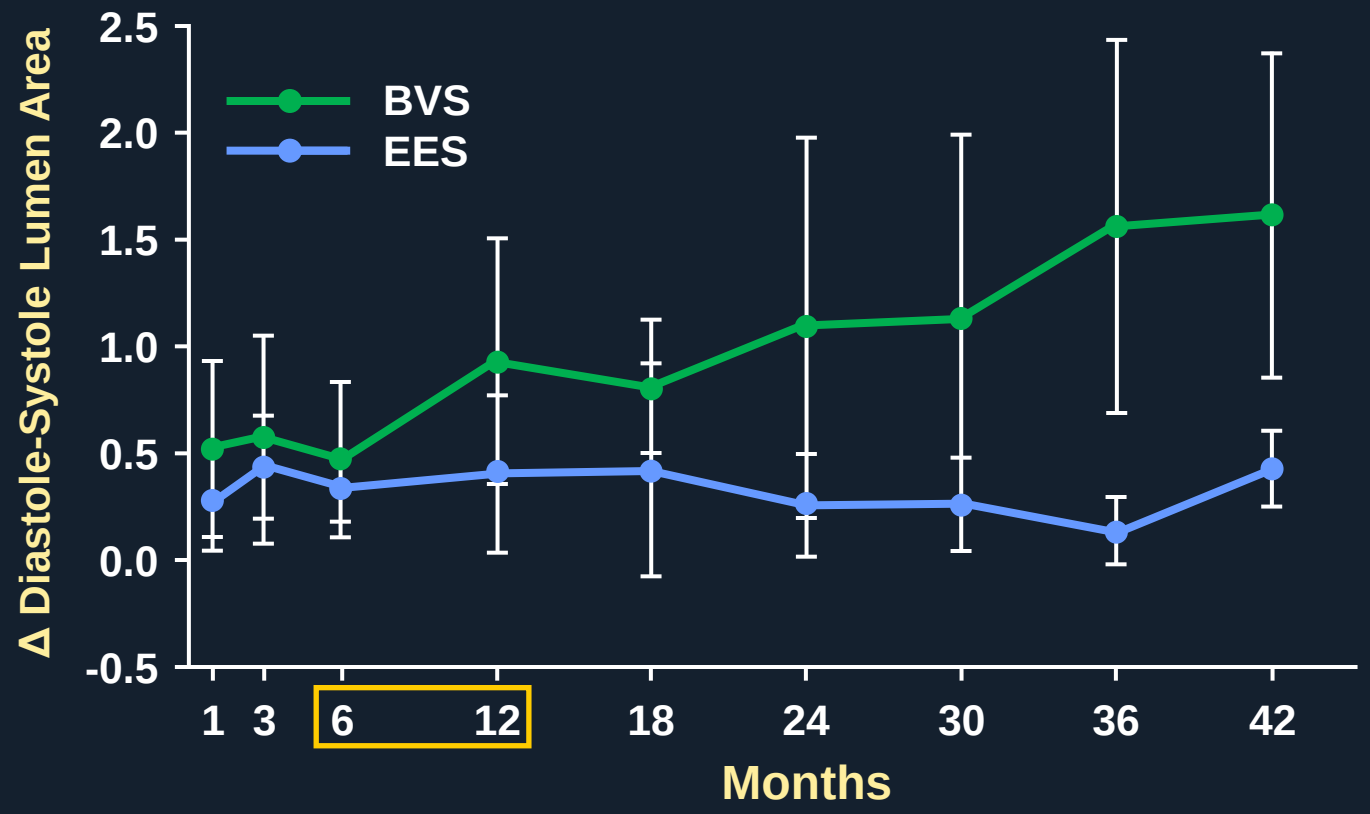
Xience V and Absorb BVS 1.1

	Macroscopic appearance	Material	Cross-section	Strut thickness
Xience V		CoCr + durable fluoropolymer		89 um
Absorb BVS 1.1		PLLA + PDLLA		157 um

Muramatsu T et al. JACC Intv 2013;6:247-57

BVS: Restoration of Pulsatility in the Porcine Coronary Model

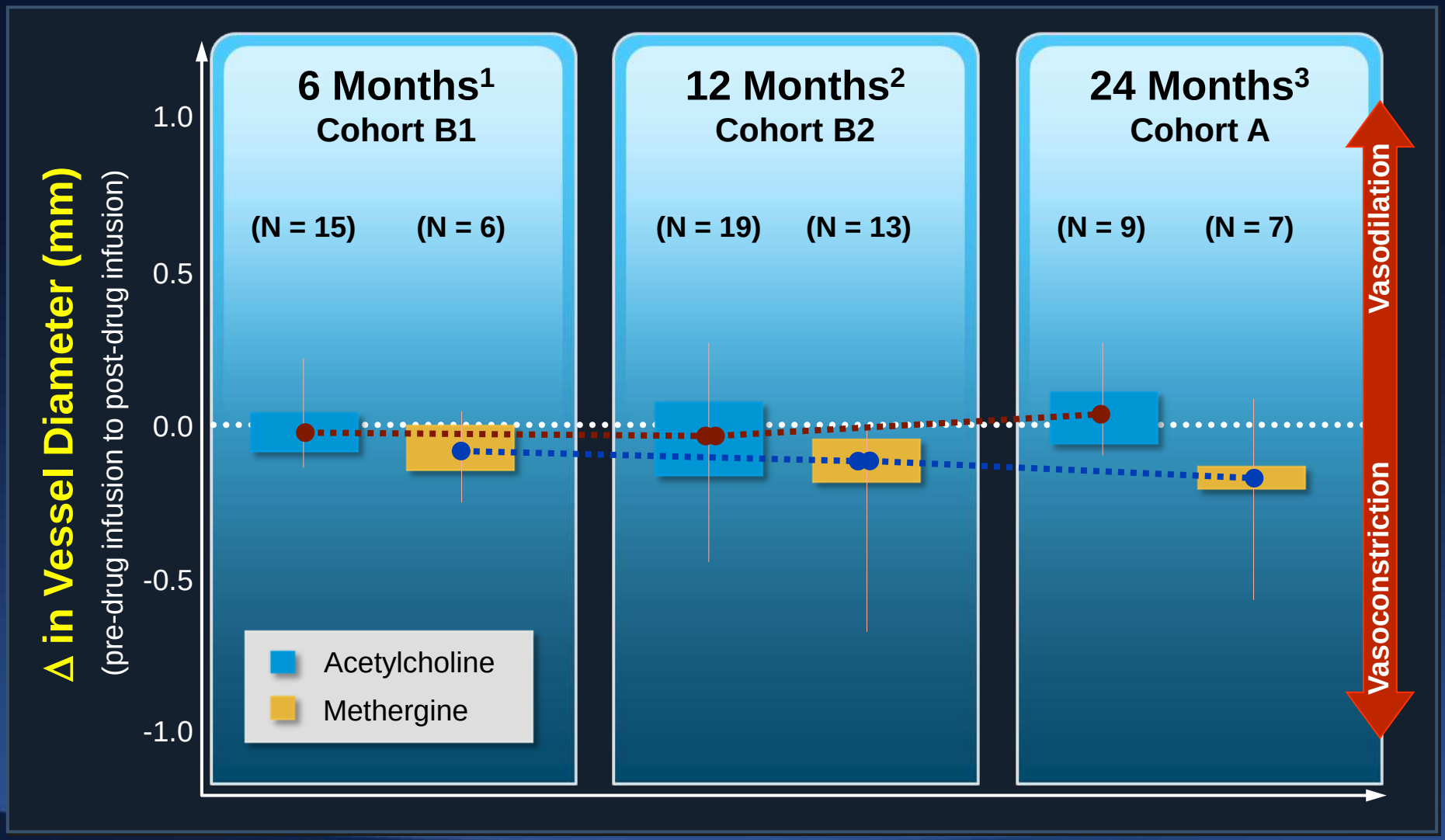




Lane JP et al. JACC Intv 2014;7:688–95

ABSORB: Vasomotion Restoration

Restoring Natural Vessel Function

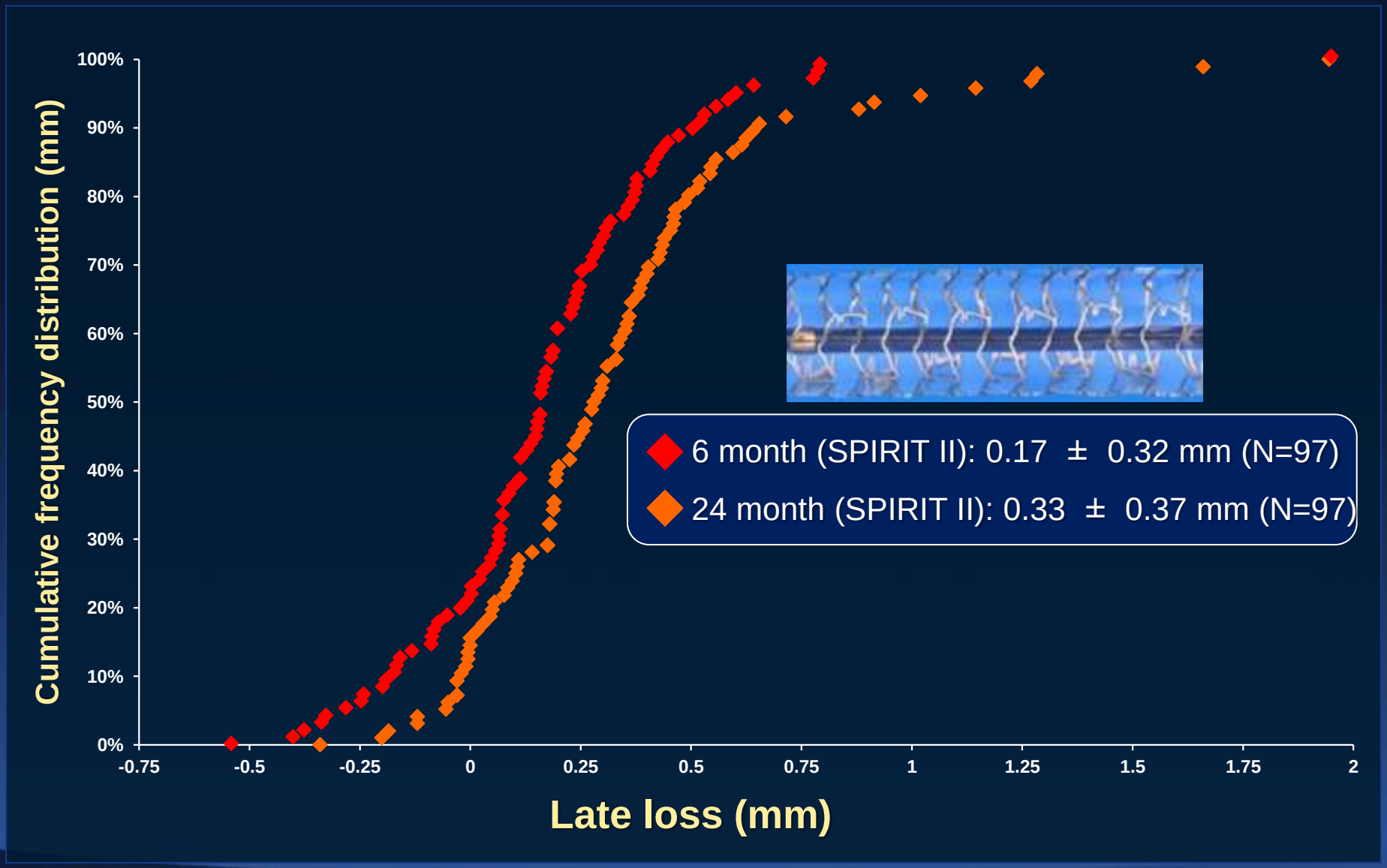


[1,2]Serruys PW. ACC 2011; [3]Serruys PW et al. *Lancet* 2009;373:897-910

Cardiovascular Research Foundation — A Passion for Innovation

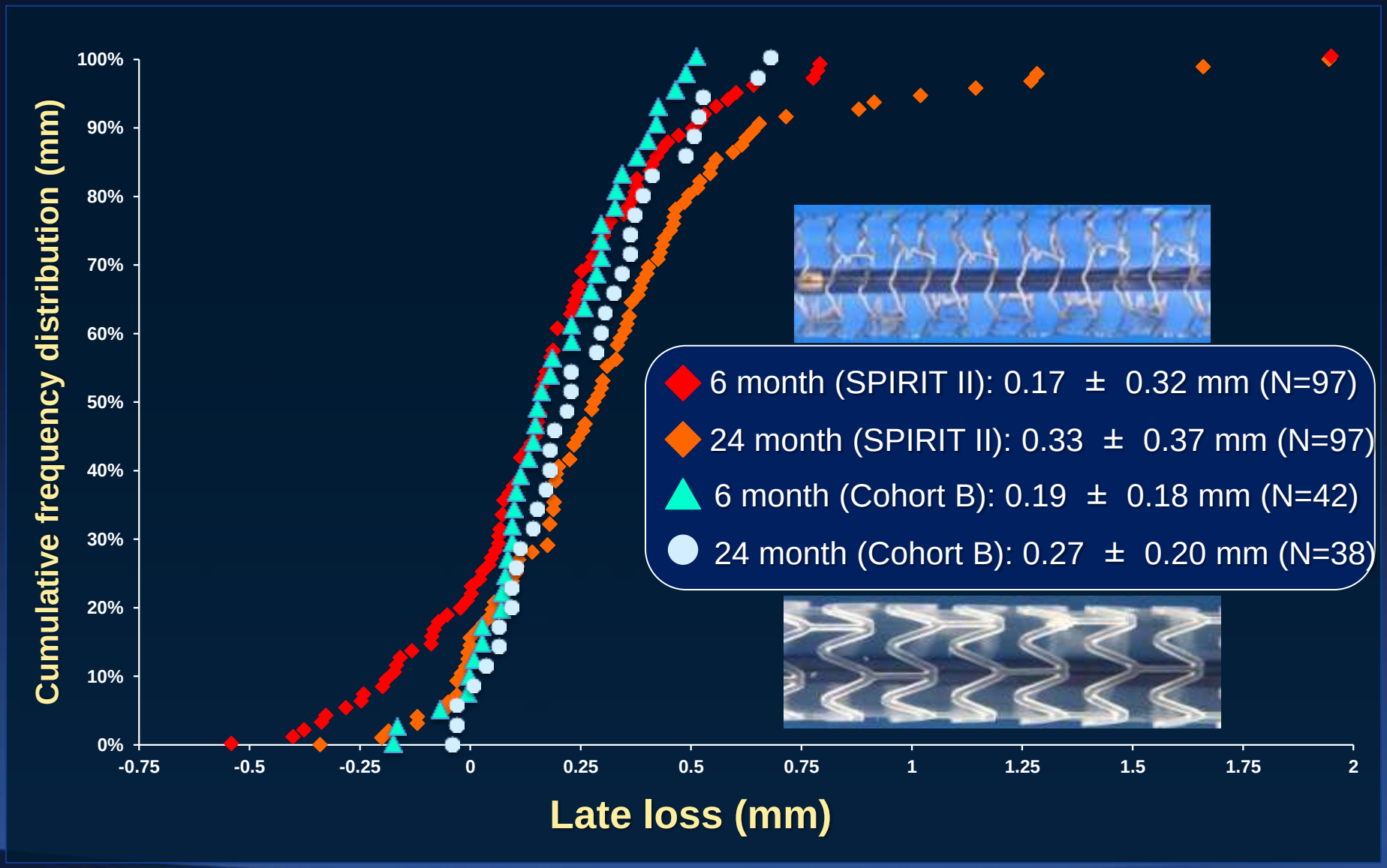
Columbia University Medical Center — NewYork-Presbyterian

Late Loss with Absorb Cohort B vs. Xience V



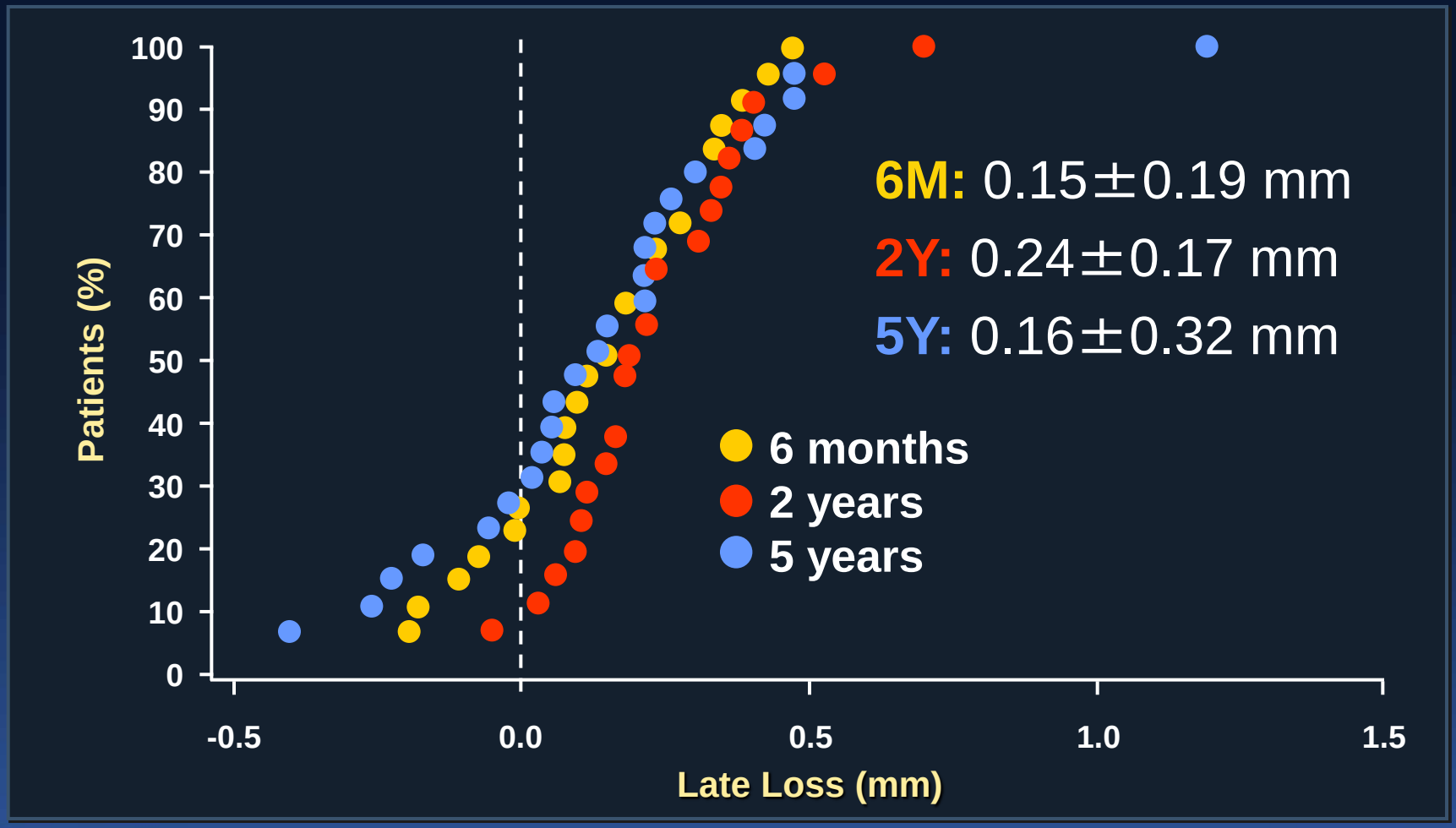
Claessen BE et al. Circ CV Int. 2009;2:339-47

Late Loss with Absorb Cohort B vs. Xience V



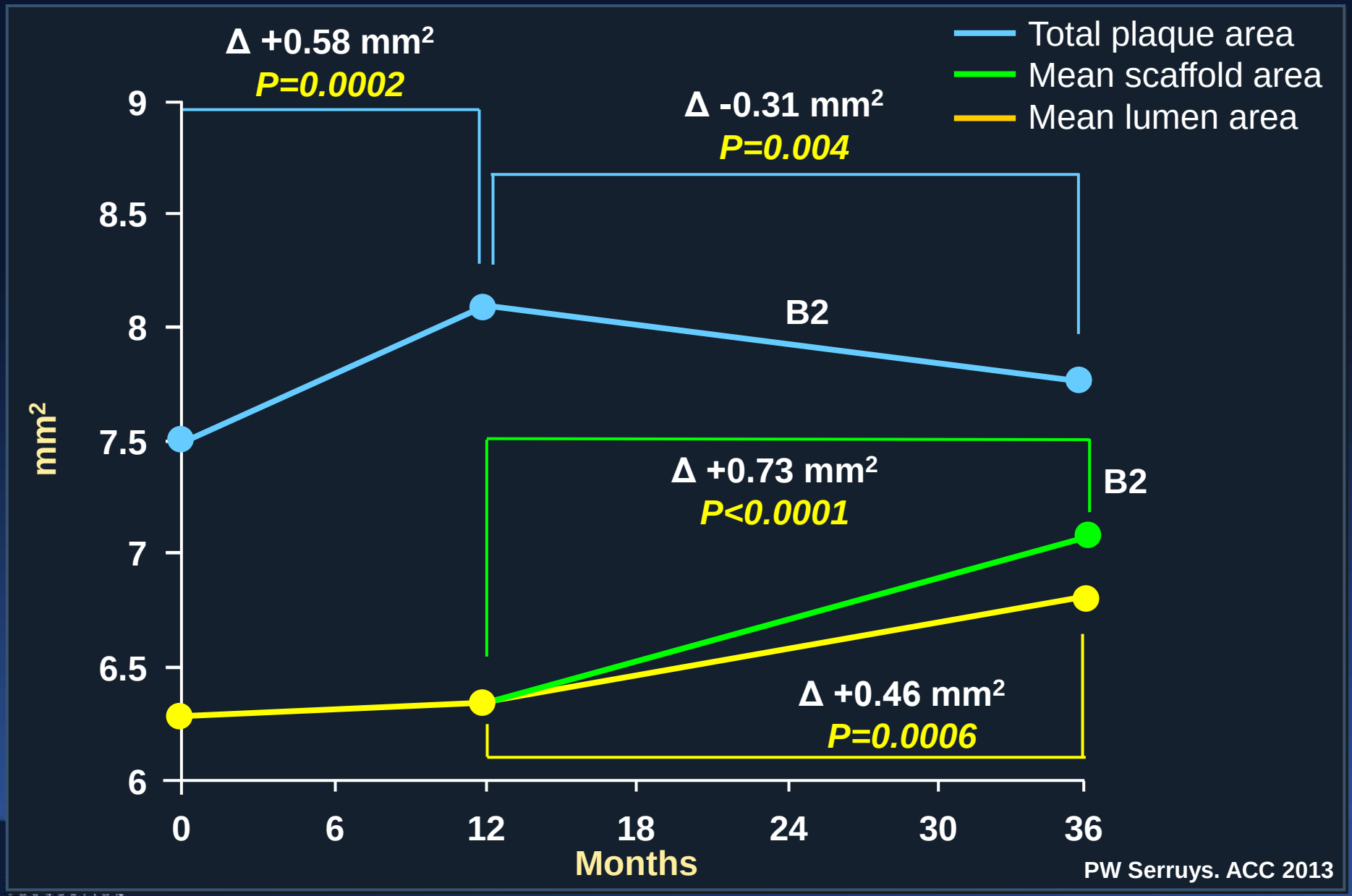
Claessen BE et al. Circ CV Int. 2009;2:339-47
Serruys PW. ESC 2012

ABSORB Cohort B1
Late Loss Through 5 Years

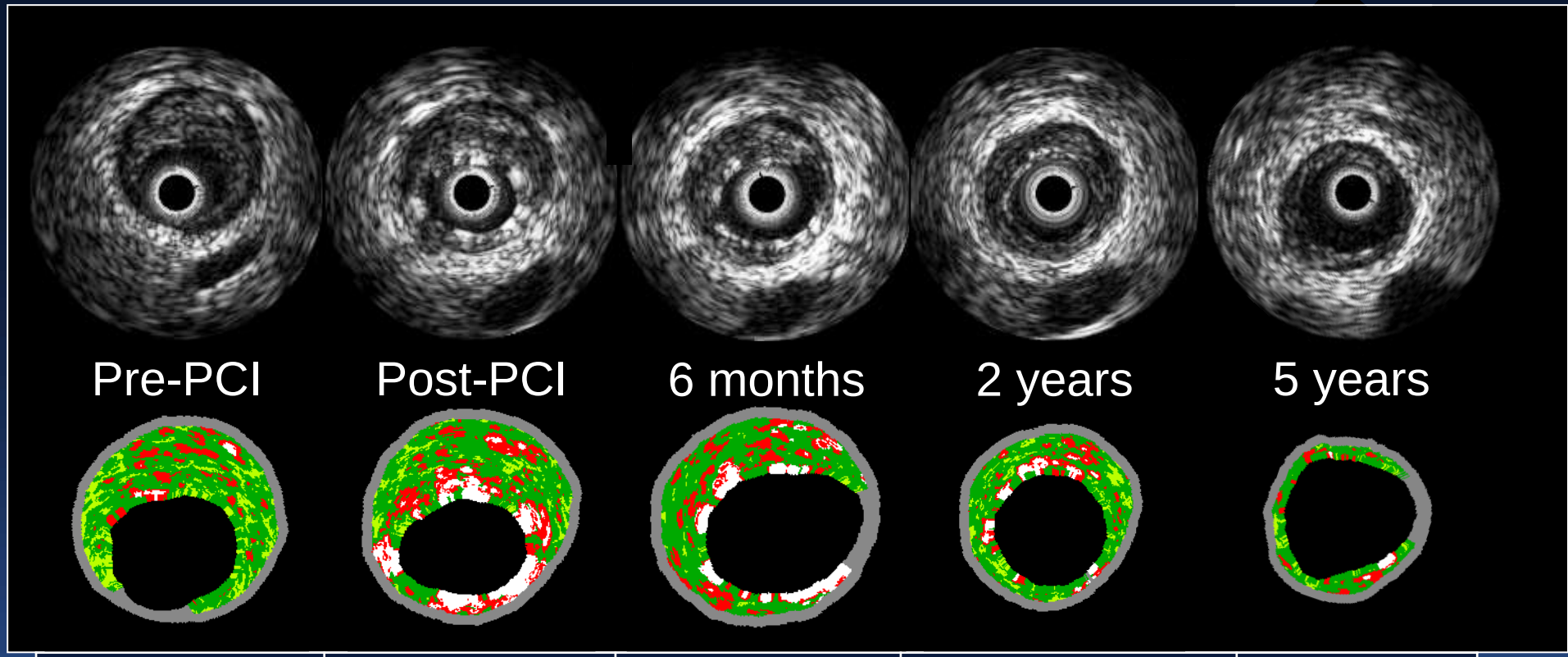


Onuma Y. TCT 2014

BVS Cohort B: Serial Quantitative IVUS (n=45)



Interventional Plaque Regression by BVS:
Substantial lumen enlargement due to plaque regression with adaptive remodeling (cohort A pt)



Vessel area (mm^2)	15.72	15.34	14.09	13.76
Mean lumen area (mm^2)	6.95	6.17	6.56	8.09
Plaque area (mm^2)	8.78	9.17	7.54	7.07

c/o Patrick Serruys

Issues of Concern with First Generation BRS

- Implant procedure
  - Profile, deliverability, visibility, overlap, retention
  - Technique more critical than w/metallic DES
  - Accurate sizing essential; ? need for imaging
  - Greater recoil?
- Greater peri-procedural MI?
- Greater stent thrombosis?

ABSORB II: 1-Year Clinical Outcomes

	Absorb 335 pts	Xience 166 pts	*P* value
Composite of cardiac death, TV-MI, clinically indicated TLR (TLF; DoCE)	4.8%	3.0%	0.35
- Cardiac death	0%	0%	1.00
- Target vessel MI	4.2%	1.2%	0.07
- Clinically indicated TLR	1.2%	1.8%	0.69
- All TLR	1.2%	1.8%	0.69
Composite all death, all MI, all revasc (PoCE)	7.3%	9.1%	0.47
- All death	0%	0.6%	0.33
- All MI	4.5%	1.2%	0.06
- All revascularization	3.6%	7.3%	0.08

Serruys PW et al. *Lancet* 2014

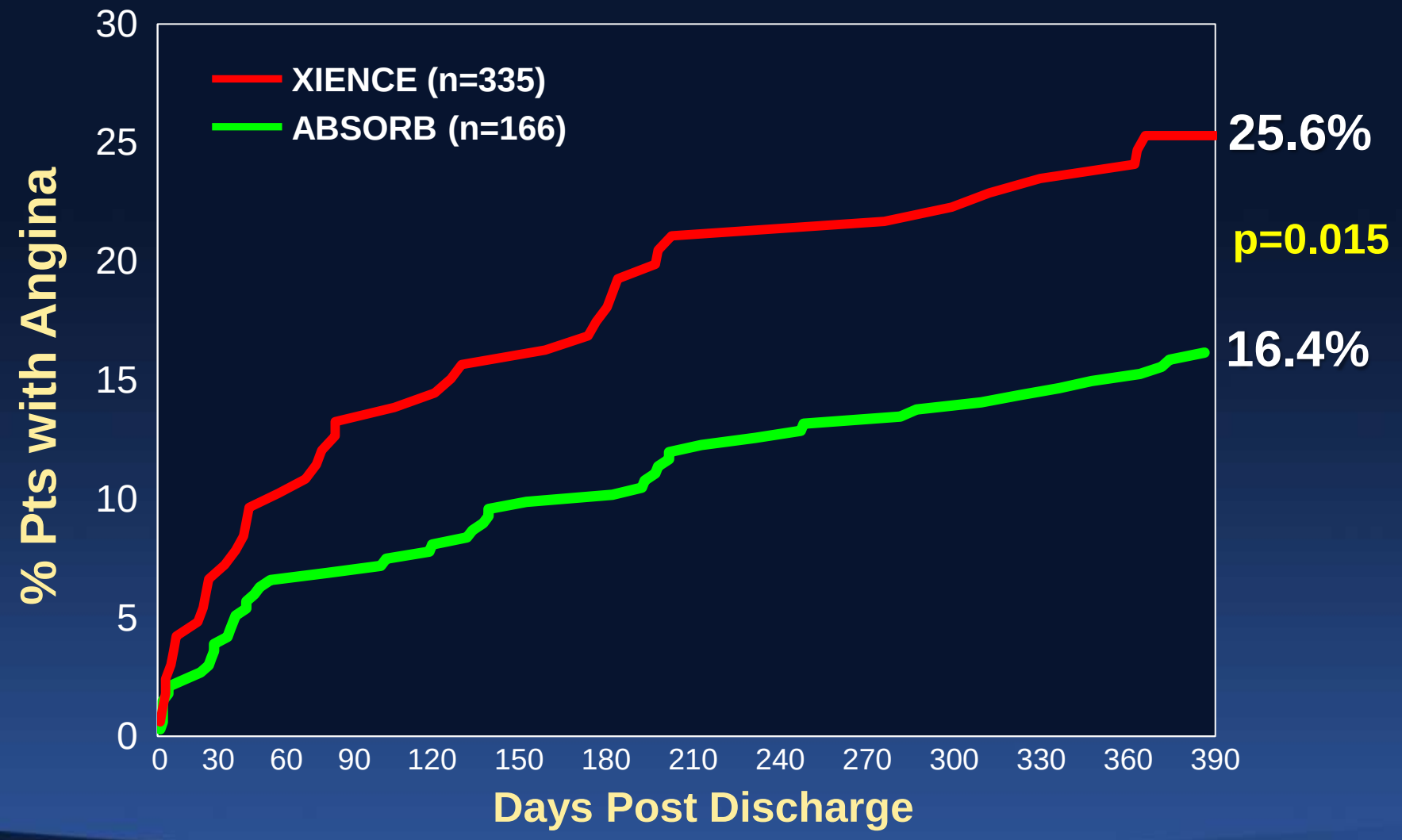
ABSORB II: Definite Scaffold/Stent Thrombosis

Cumulative incidence in percentage	Absorb 335 pts	Xience 166 pts	*P* value
Definite scaffold/stent thrombosis			
- Acute (0-1 day)	0.3% (1 pt)	0.0	1.0
- Sub-acute (2–30 days)	0.3% (1 pt)	0.0	1.0
- Late (31–365 days)	0.0	0.0	-
Probable scaffold/stent thrombosis			
- Acute (0-1 day)	0.0	0.0	-
- Sub-acute (2–30 days)	0.0	0.0	-
- Late (31–365 days)	0.3% (1 pt)	0.0	1.0
Definite or probable scaffold/stent thrombosis	0.9% (3 pts)	0.0	0.55

Serruys PW et al. *Lancet* 2014

ABSORB II: Time to first occurrence of angina

(excluding first 7 days post randomization)



Serruys PW et al. *Lancet* 2014

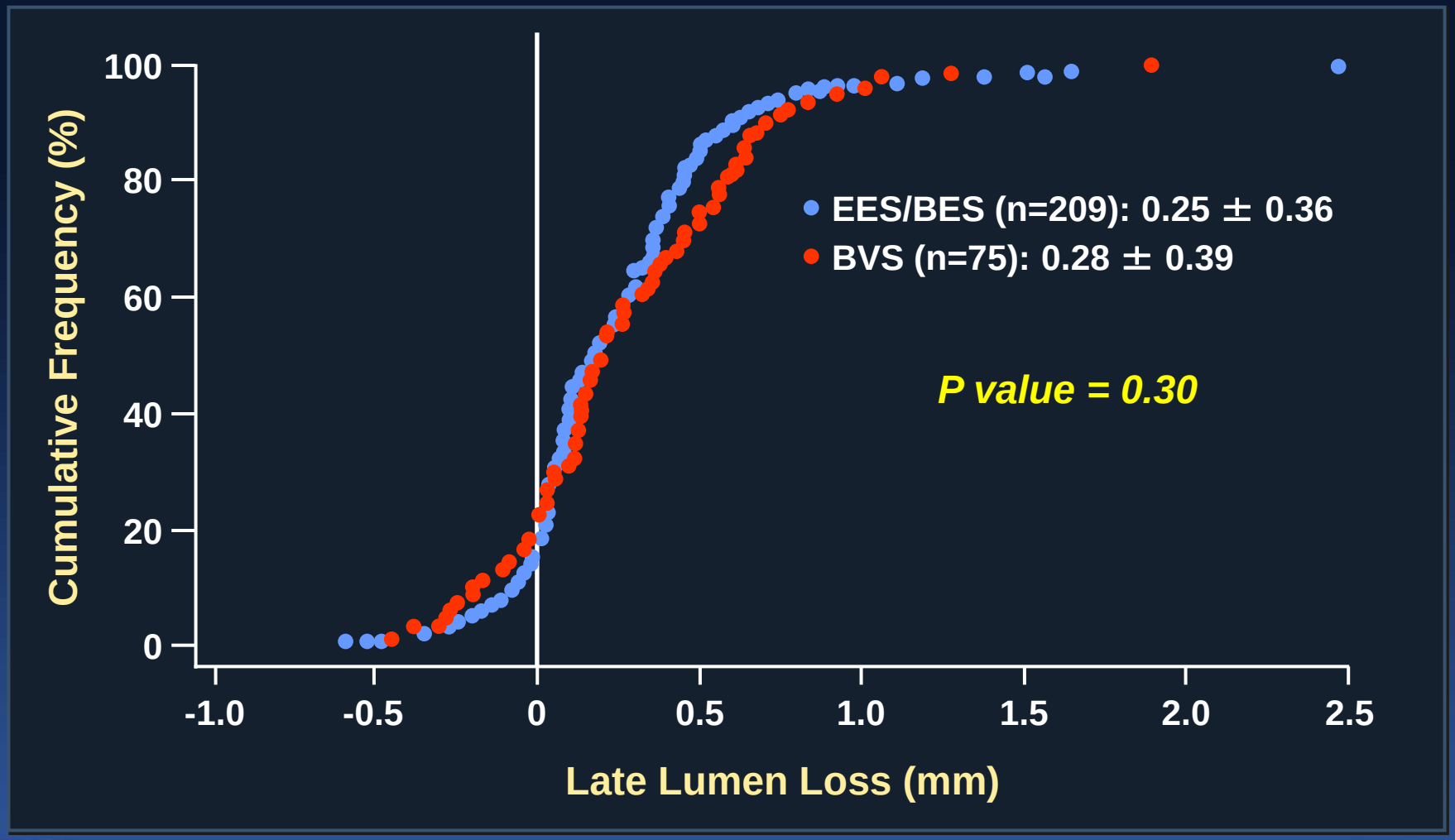
ABSORB II: Medication and Exercise Testing

	6 months			12 months		
	Absorb 335 pts	Xience 166 pts	*P*	Absorb 335 pts	Xience 166 pts	*P*
Anti-angina medications, %						
- Beta-blockers	71.0	67.9	0.48	70.5	65.9	0.29
- Calcium channel blockers	20.8	21.2	0.92	23.7	23.2	0.89
- Nitrates	**17.8**	**26.7**	**0.02**	19.5	26.2	0.09
- Dual antiplatelet therapy	97.3	97.0	1.00	82.8	83.1	0.93
Exercise test performed, %	91.9	94.6	0.28	86.0	85.5	0.9
- Maximal HR (beats/min)	132	132	0.93	133	135	0.38
- Maximal workload (METS)	9.02	9.05	0.95	9.32	9.41	0.83
- Exercise duration (mins)	8.10	8.53	0.22	8.55	8.99	0.26
- ≥0.1 mV ST depression or chest pain, %	18.2	20.4	0.57	15.0	15.5	0.9
Terminated due to >0.2 mV ST depression, %	**4.3**	**17.2**	**0.05**	4.9	5.9	1.0

Serruys PW et al. *Lancet* 2014

EVERBIO II: 240 pts ranromized 1:1:1 at a single center to EES, BES or Absorb BVS

1° EP: 9-month in-stent late lumen loss (mm)

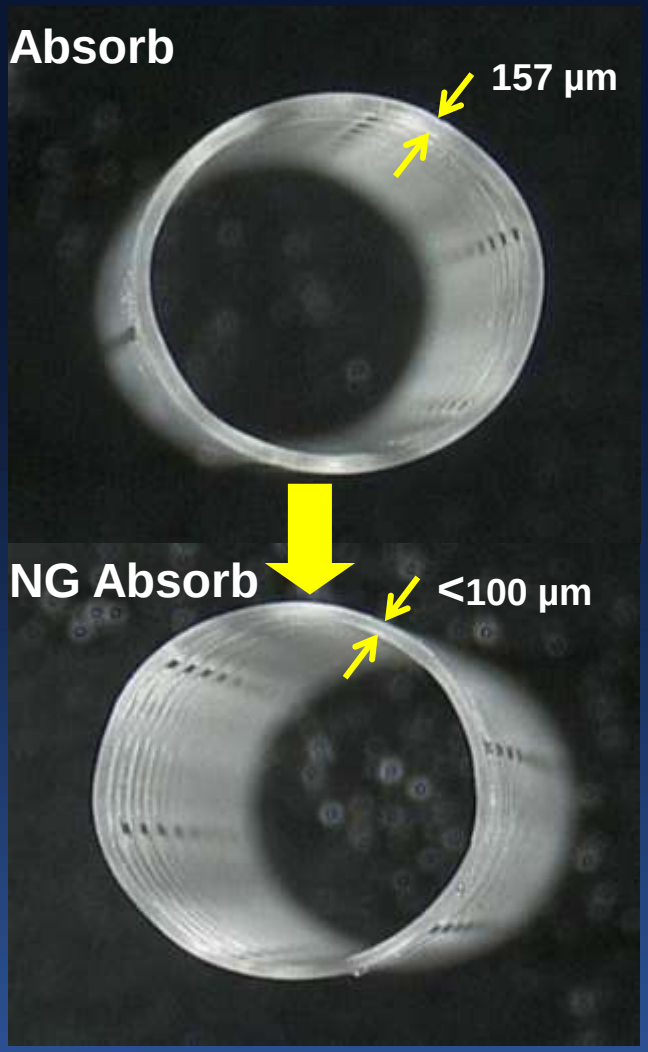


Puricel S et al. *JACC* 2015;65:791–801

Upcoming ABSORB RCTs (Fall 2015)

- ABSORB China, n=480
- ABSORB Japan, n=400
- ABSORB III, n=2,000
- TROFI II (STEMI), n=190

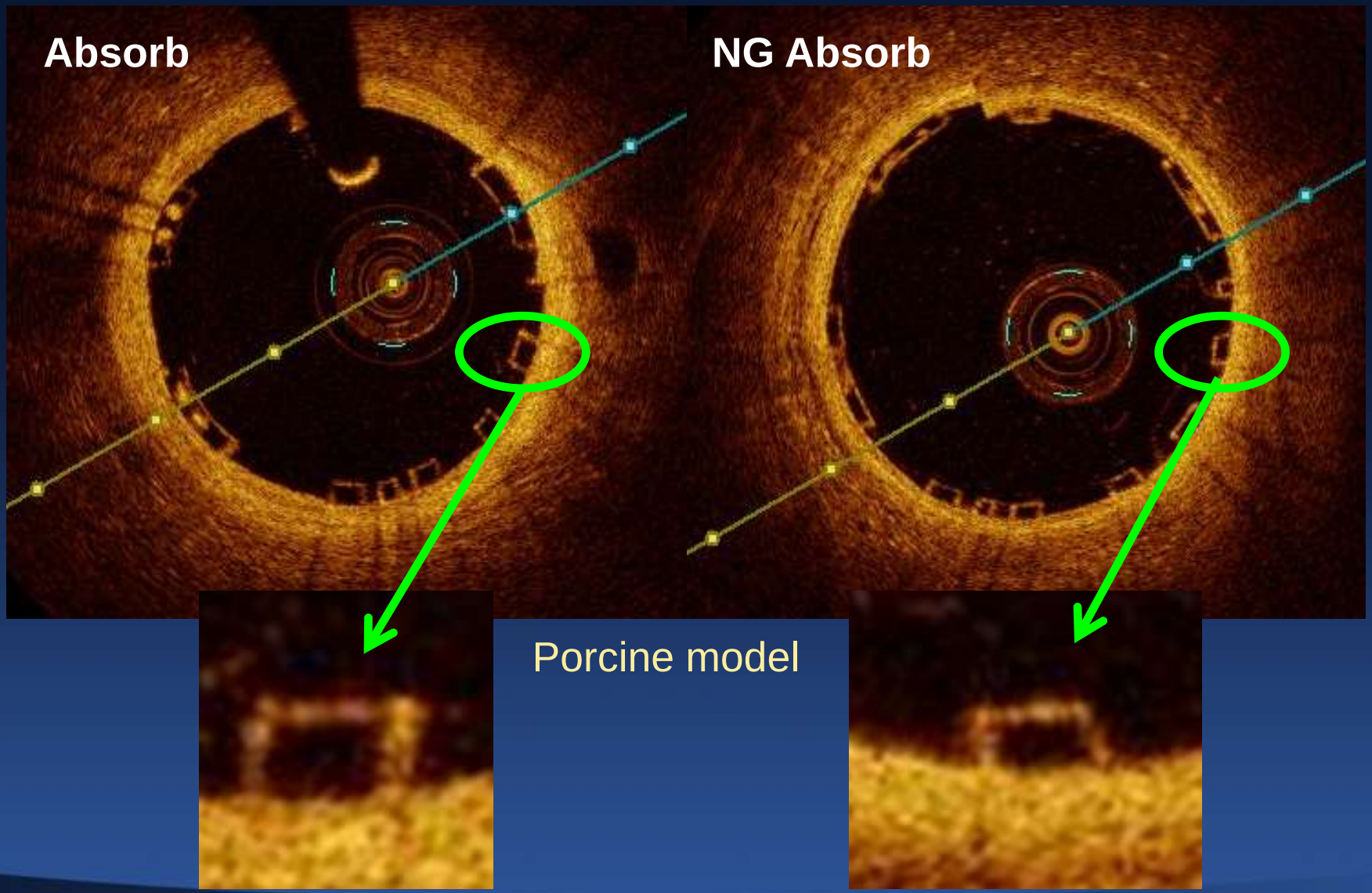
Next Generation Absorb Scaffold



- Thinner struts: <100 microns
- Expanded range of diameters and lengths
- Larger expansion limit: ≥0.75mm over nominal
- Broader pressure working range: ¼ size at least 16 atm
- Shorter resorption time
- Unchanged:
  - Drug content & elution rate
  - Pattern & footprint
  - Radial strength
  - Scaffold retention

Data on file at Abbott Vascular

Next Generation Absorb Scaffold

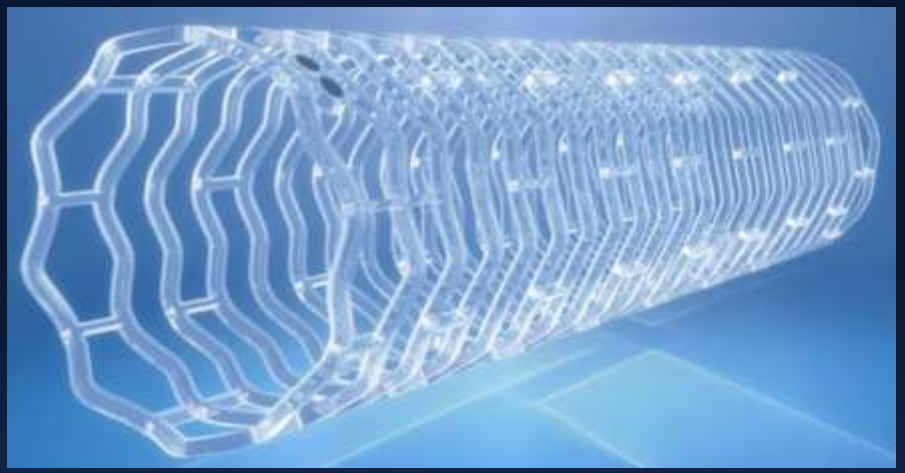


Data on file at Abbott Vascular

DESolve Bioresorbable Coronary Scaffold

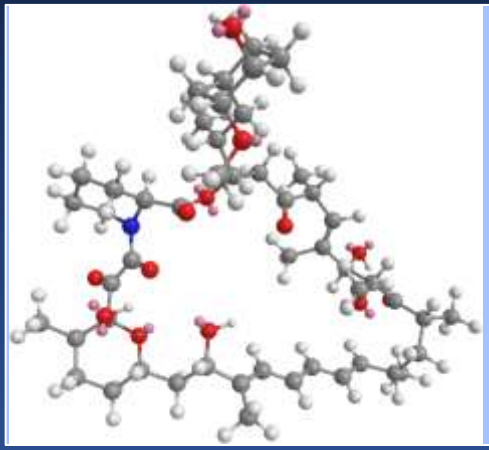
DESolve

Novolimus-eluting PLLA-based polymer scaffold



Novolimus

a major metabolite of sirolimus



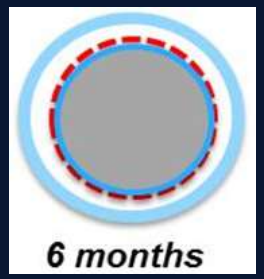
Formula:
$C_{50}H_{77}NO_{13}$
MW: 900

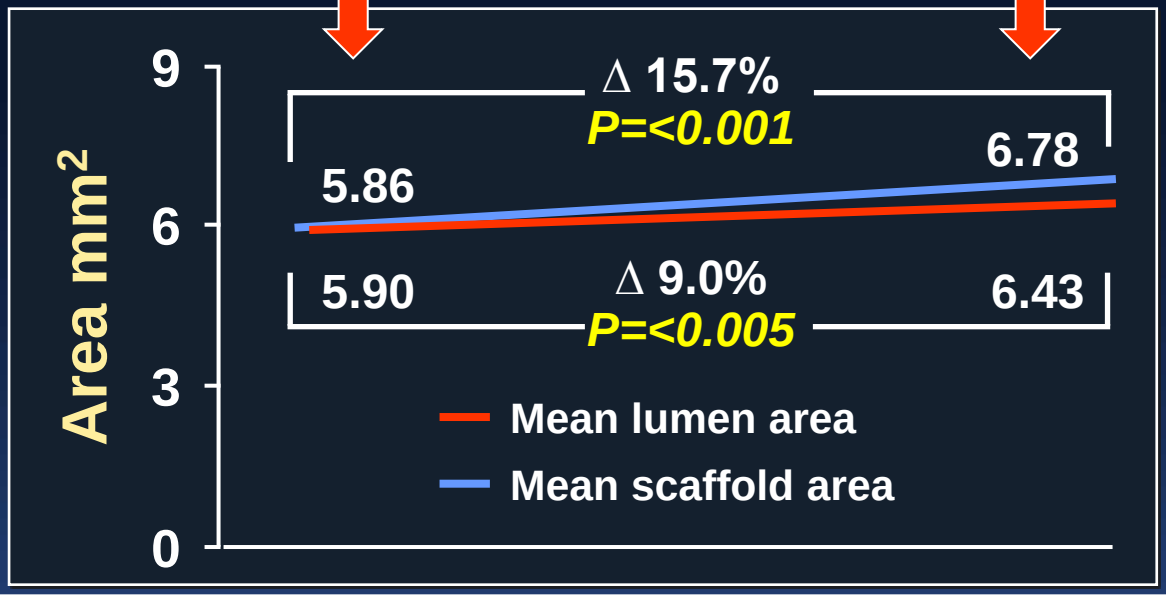
DESolve is CE Mark approved; not available for sale in the US

Abizaid A. TCT 2014

DESolve Nx Serial IVUS: 6 Months

$N_L = 40$





% volume obstruction	–	5.05 ± 4.20
ISA (n)	3	1
ISA Volume (mm^3)	0.70 ± 0.17	0.10

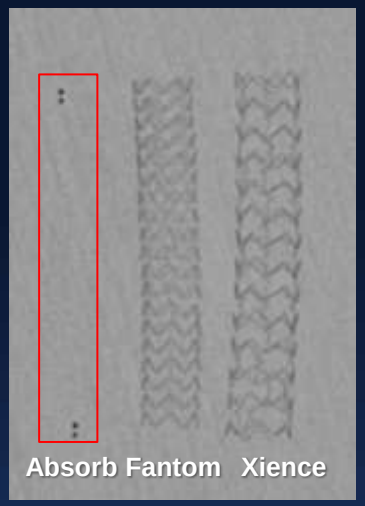
1 persistent early ISA; No late acquired ISA or aneurysm formation

Abizaid A. TCT 2014

Reva *Fantom* Sirolimus-Eluting Bioresorbable Scaffold

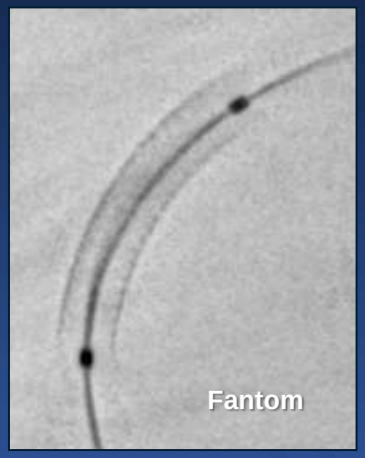
Desaminotyrosine-Derived Polycarbonate

Radio-opacity similar to metallic DES



3.0mm Nominal Device

Capable of expansion to >4.8mm without fracture



Polymer vs Metal Properties

Polymer/ metal	Tensile modulus of elasticity (Gpa)	Tensile strength (Mpa)	Elongation at break (%)	Degradation time (months)
Poly(L-lactide)	3.1 - 3.7	60 - 70	2-6	24 - 36 mos
Poly (DL-lactide)	3.1 - 3.7	45 - 55	2-6	6 - 12
Cobalt chromium	210 - 235	1449	~40	Biostable
Magnesium alloy	40 - 45	220 - 330	2 - 20	1 - 12 mos
Iron alloy	200	300	23	>4 years

Modified from Onuma, et al. Circulation 2011

Conclusions

Bioresorbable scaffolds in a nutshell

- By restoring cyclic pulsatility and normal vasomotion, enabling adaptive vascular remodeling, promoting plaque regression and removing the nidus for late adverse events, BRS offer the potential to improve clinical outcomes compared to metallic DES
- First generation BRS technology has significant design-related limitations compared to state-of-the-art metallic DES, placing a premium on optimal procedural technique, without which early and late adverse events may be increased; the technology is rapidly improving
- Adequately powered RCTs are required to demonstrate whether BRS are noninferior or superior to metallic DES