From ABSORB Cohort A to ABSORB III and IV Randomized Trials

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Director Invasive Services
Co-Director Cardiac Gene Bank

Cleveland Clinic

Disclosures

- Consultant, Abbott Vascular
- Co-Principal Investigator, ABSORB III and IV

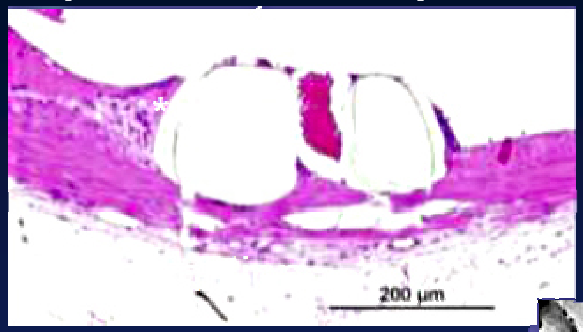
Bioabsorbable Coronary Scaffold

Potential Benefits

- Minimize Neoatherosclerosis -> Less late stent thrombosis
- Restore normal vasomotor responses -> Less low shear distally -> less atherosclerosis; better peak exercise capacity
- Doesn’t block CABG (esp LIMA to LAD)
- Allows better non-invasive CT evaluation

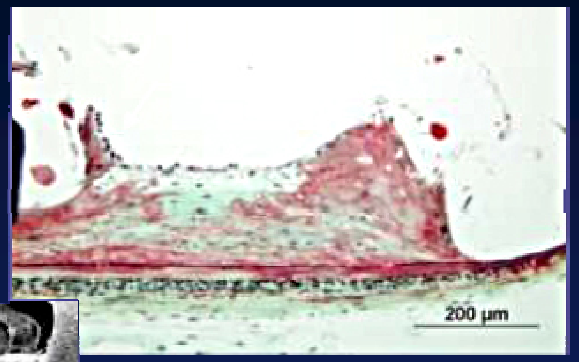
Delayed Healing - DES

Lack of neointimal growth (uncovered struts)



Rabbit 28 days

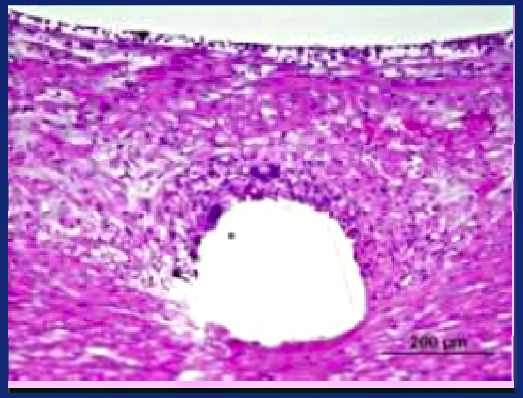
Persistent fibrin deposition



CYPHER

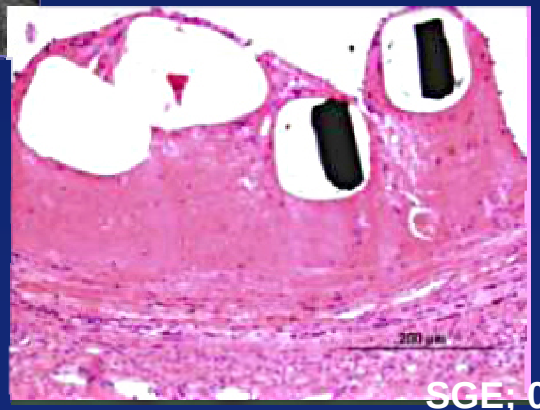
TAXUS

Severe inflammation



Porcine 28 days

Fibrin deposition with stent malapposition

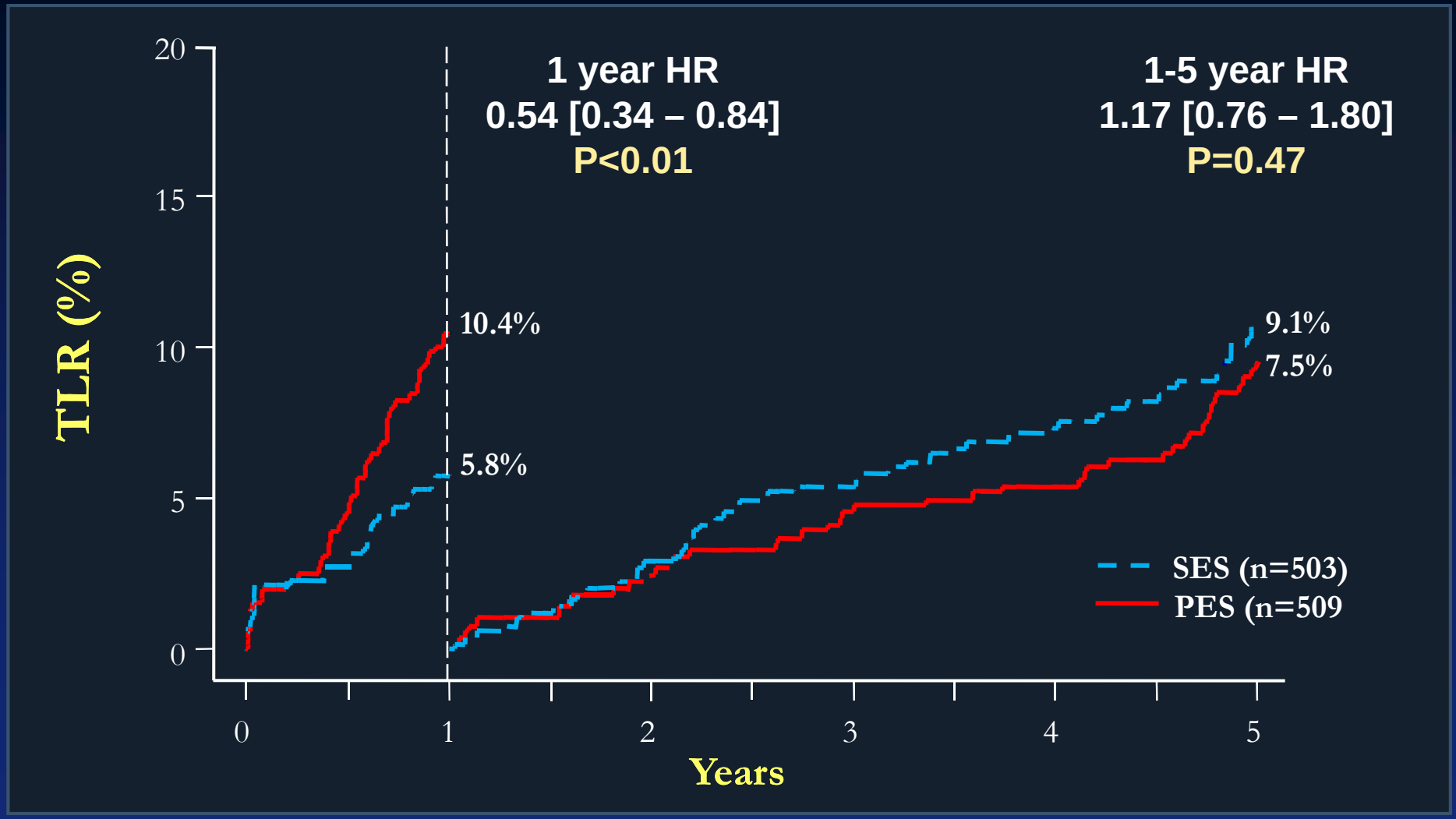


Virmani et al.

SGE; 0212-6, 66

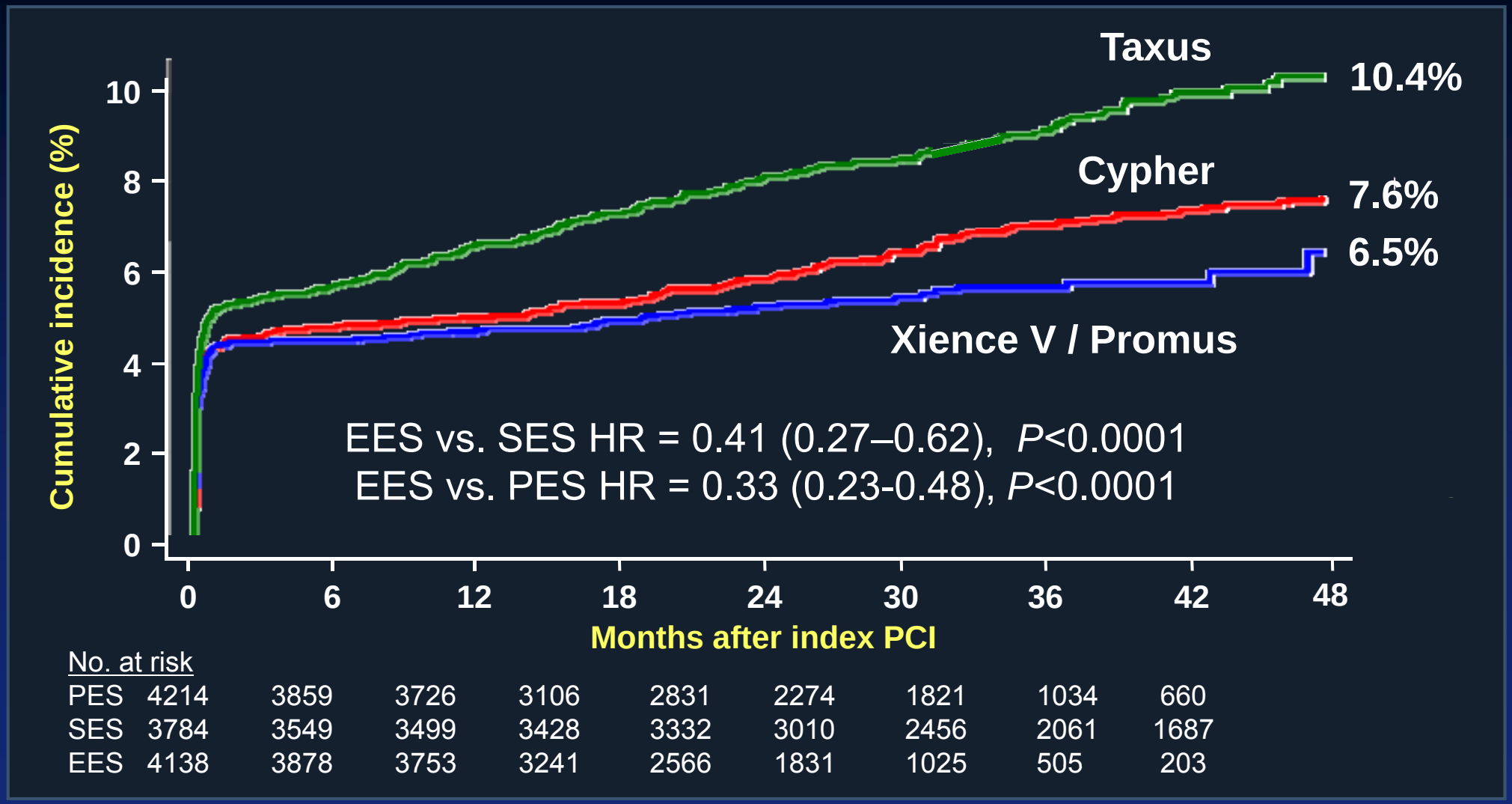
SIRTAX-LATE: Target Lesion Revascularization

Landmark analysis



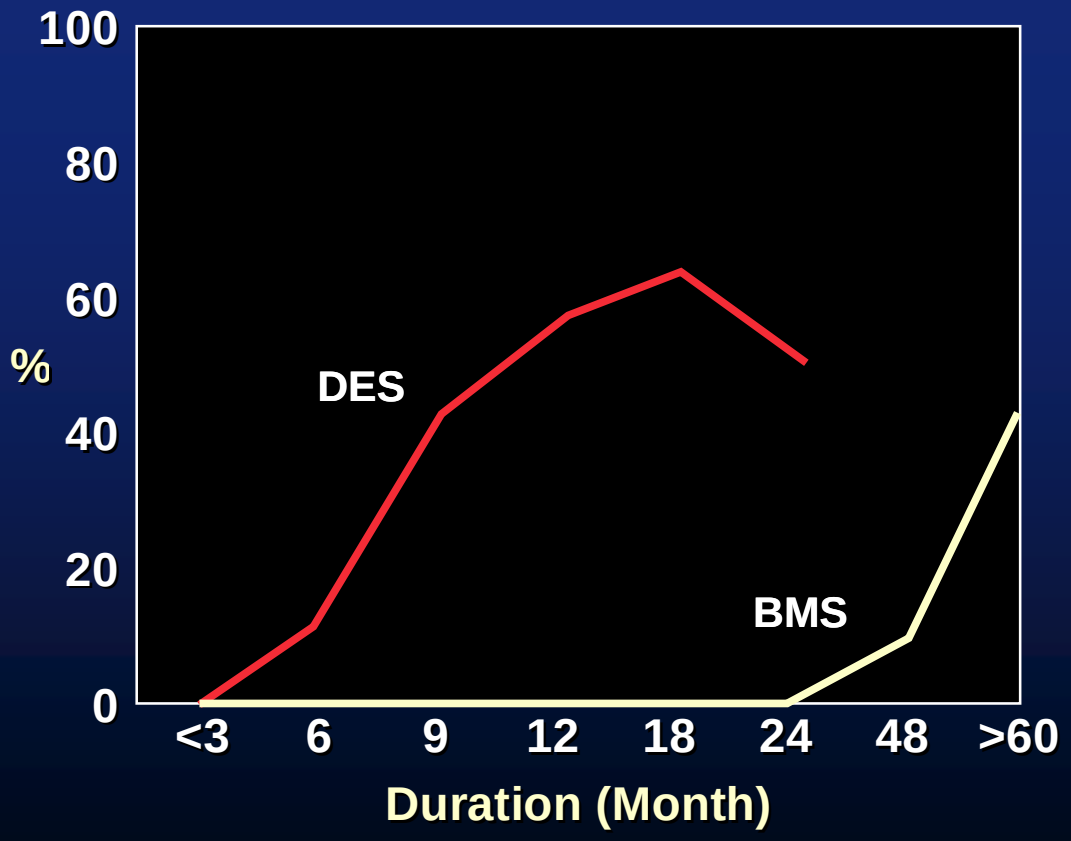
Raber L et al. *Circulation*. 2011;123:2819-2828

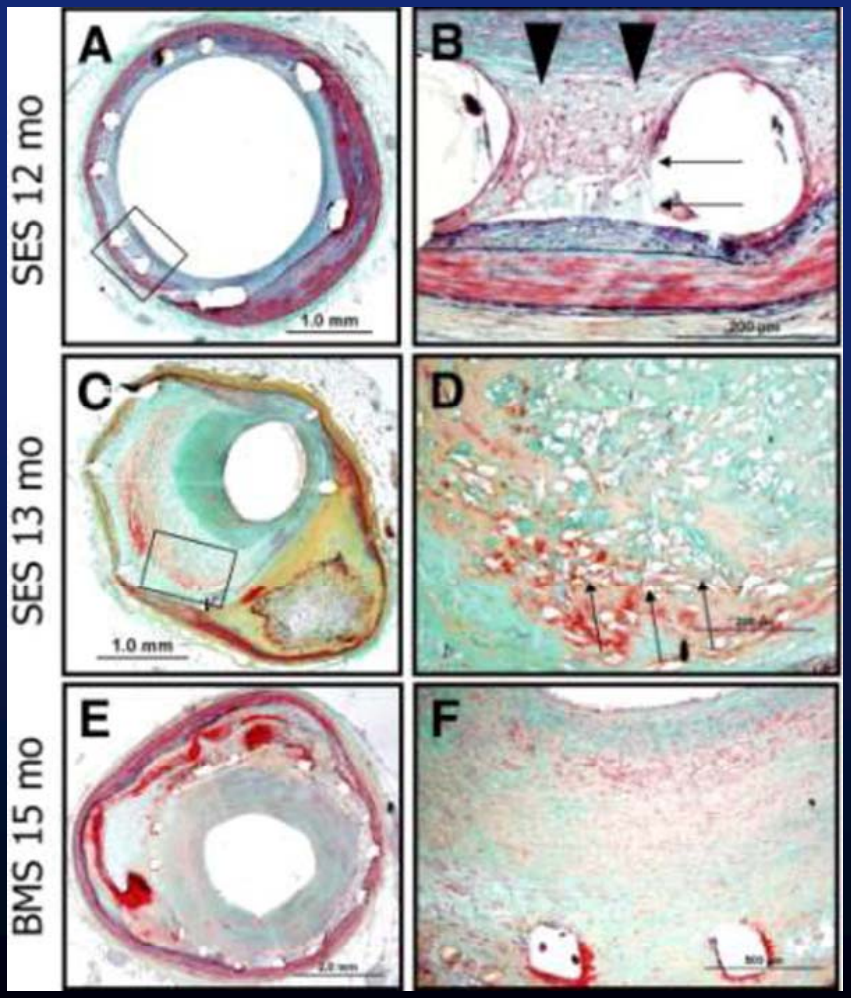
Bern Rotterdam (n=12,339 pts)
ARC Definite or Probable ST at 4 Years



Lorenz Ršber, ESC 2011

Neoatherosclerosis and Time From Stent Implant

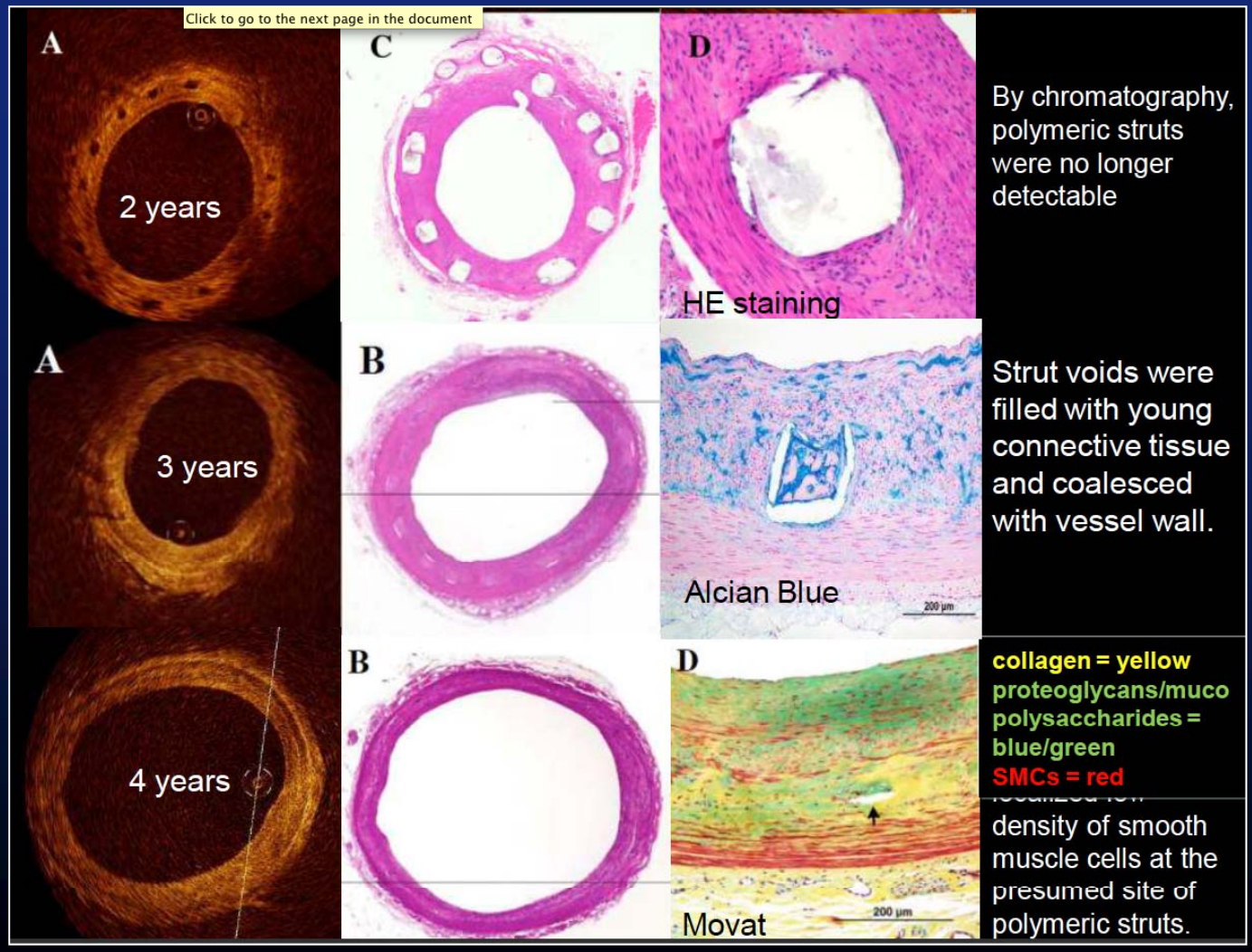




Nakazawa et al., JACC Img 2009;2:625-8

SGE; 0412-10, 11

BVS: Absorption Seen by OCT and Pathology



Serruys et al., the Netherlands, 2011

Abbott BVS

Expectations

- Parity versus current DES early
- Superiority versus DES late

ABSORB Global Clinical Program

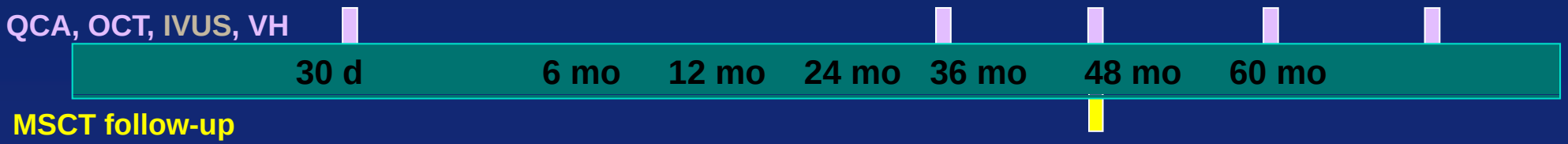
Building the Evidence

ABSORB Cohort A

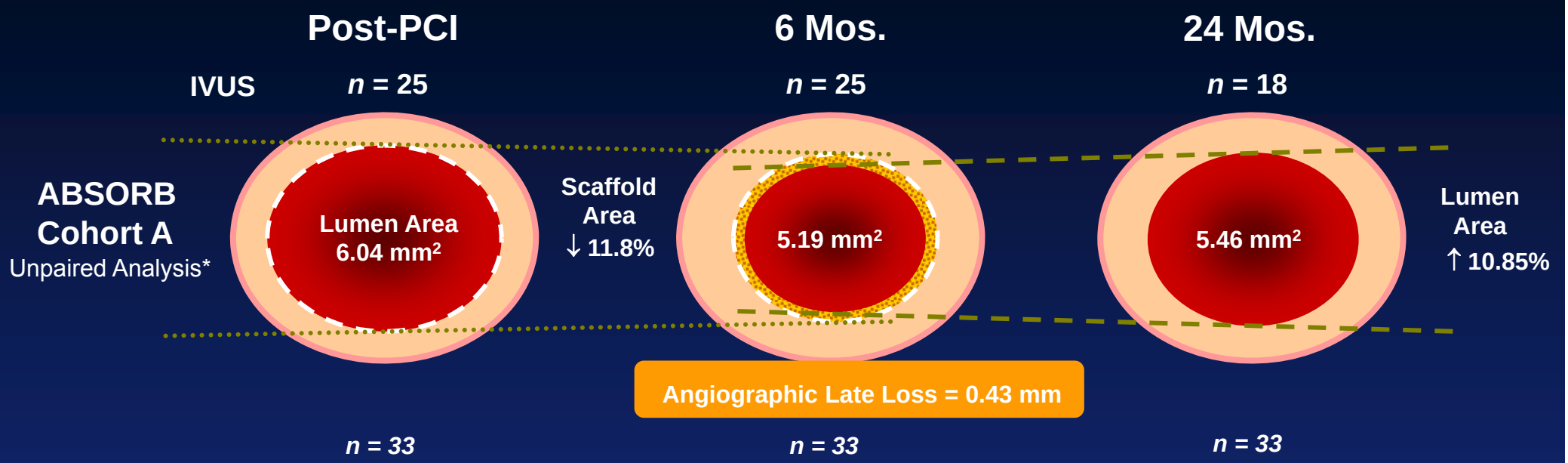
Principal Investigators:

Patrick Serruys, John Ormiston

- **Prospective, open label, single arm study**
- **30 patients enrolled at 4 sites**
- **Device sizes: 3.0 x 12 mm; 3.0 x 18 mm in two patients**
- **Treatment: single *de novo* lesion**
- **Follow-up schedule:**



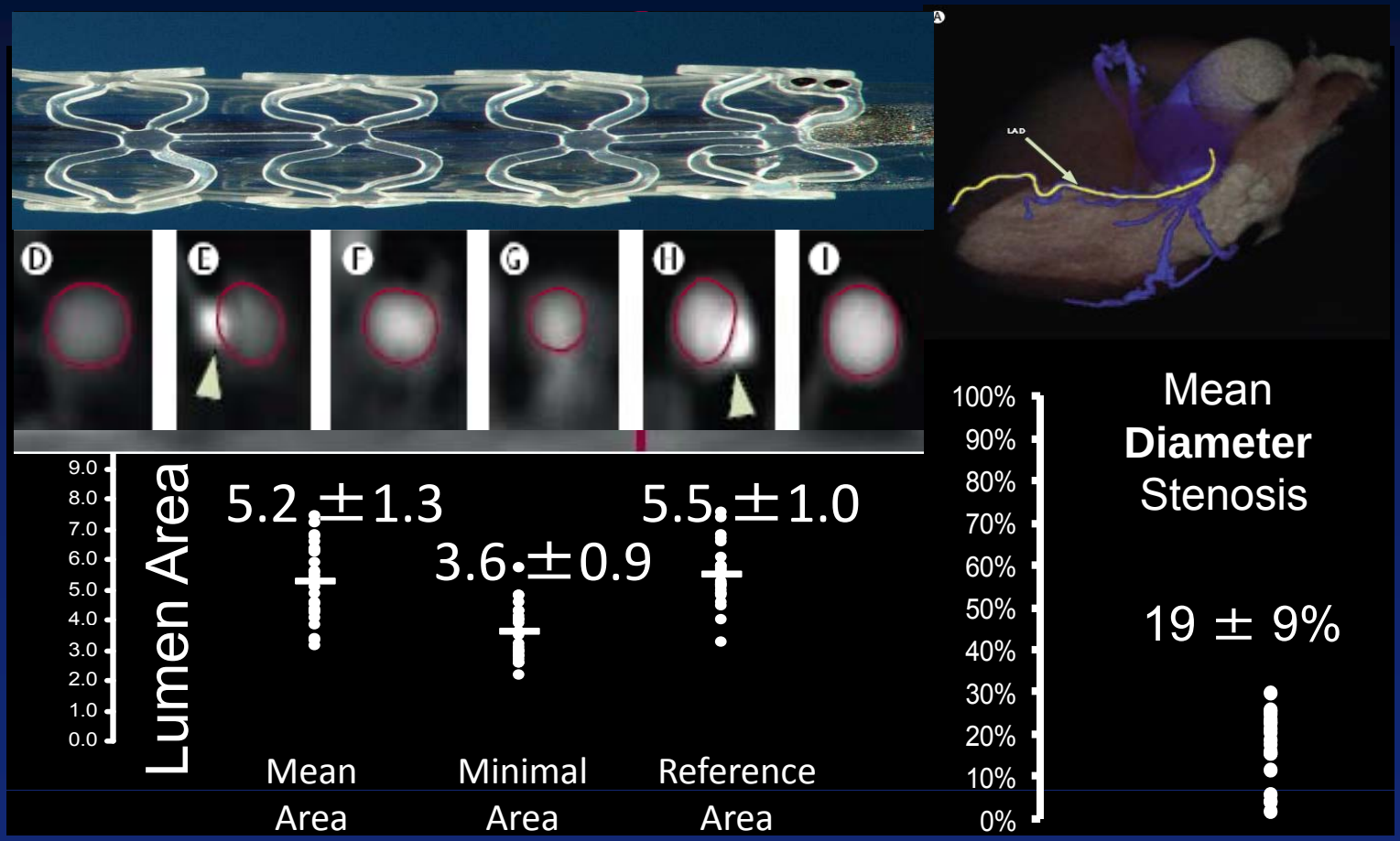
ABSORB Cohort A
Temporal Changes in Lumen



- Late lumen loss at 6 months mainly due to reduction in scaffold area
- Very late lumen enlargement noted from 6 months to 2 years

*Serruys, PW., TCT 2008

Non-invasive CT imaging for early and late follow-up is now feasible



Serruys, PW, PCR, 2010

ABSORB A – 5Y Clinical Results

Hierarchical	6 Months 30 Patients	12 Months 29 Patients*	5 Years 29 Patients*
Ischemia Driven MACE, %(n)	3.3% (1)*	3.4% (1)**	3.4% (1)**
Cardiac Death, %	0.0%	0.0%	0.0%
MI, %(n)			
Q-Wave MI	0.0%	0.0%	0.0%
Non Q-Wave MI	3.3% (1)*	3.4% (1)**	3.4% (1)**
Ischemia Driven TLR , %			
by PCI	0.0%	0.0%	0.0%
by CABG	0.0%	0.0%	0.0%

- No new MACE events between 6 months and 5 years
- No scaffold thrombosis up to 5 years

*consent withdrawn after 6 months; **Non-ID-TLR (DS<42%) w/ post-procedural non-Q MI

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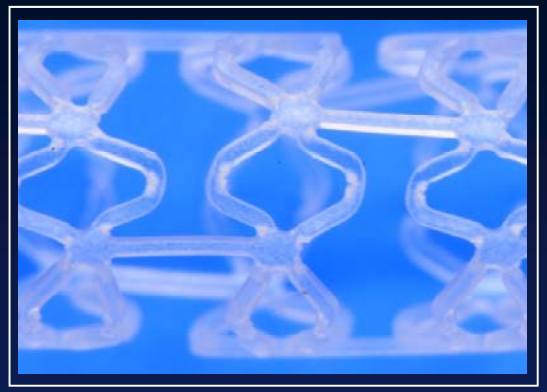
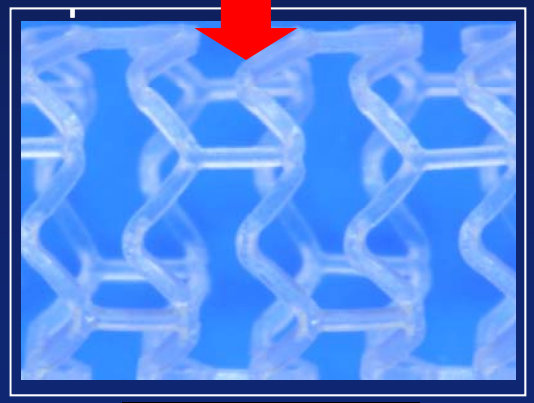
Device Optimization Objectives



Cohort A



Cohort B

- More uniform strut distribution
- More even support of arterial wall
- Maintain radial strength for at least 3-4 months
- Storage at room temperature
- Improved device retention
- Unchanged:
  - Material, coating and backbone
  - Strut thickness
  - Drug release profile
  - Total degradation Time

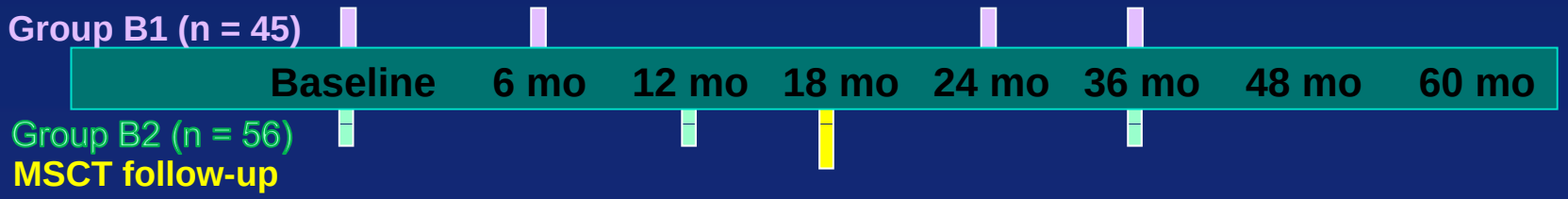
Photos taken by and on file at Abbott Vascular.

ABSORB Cohort B

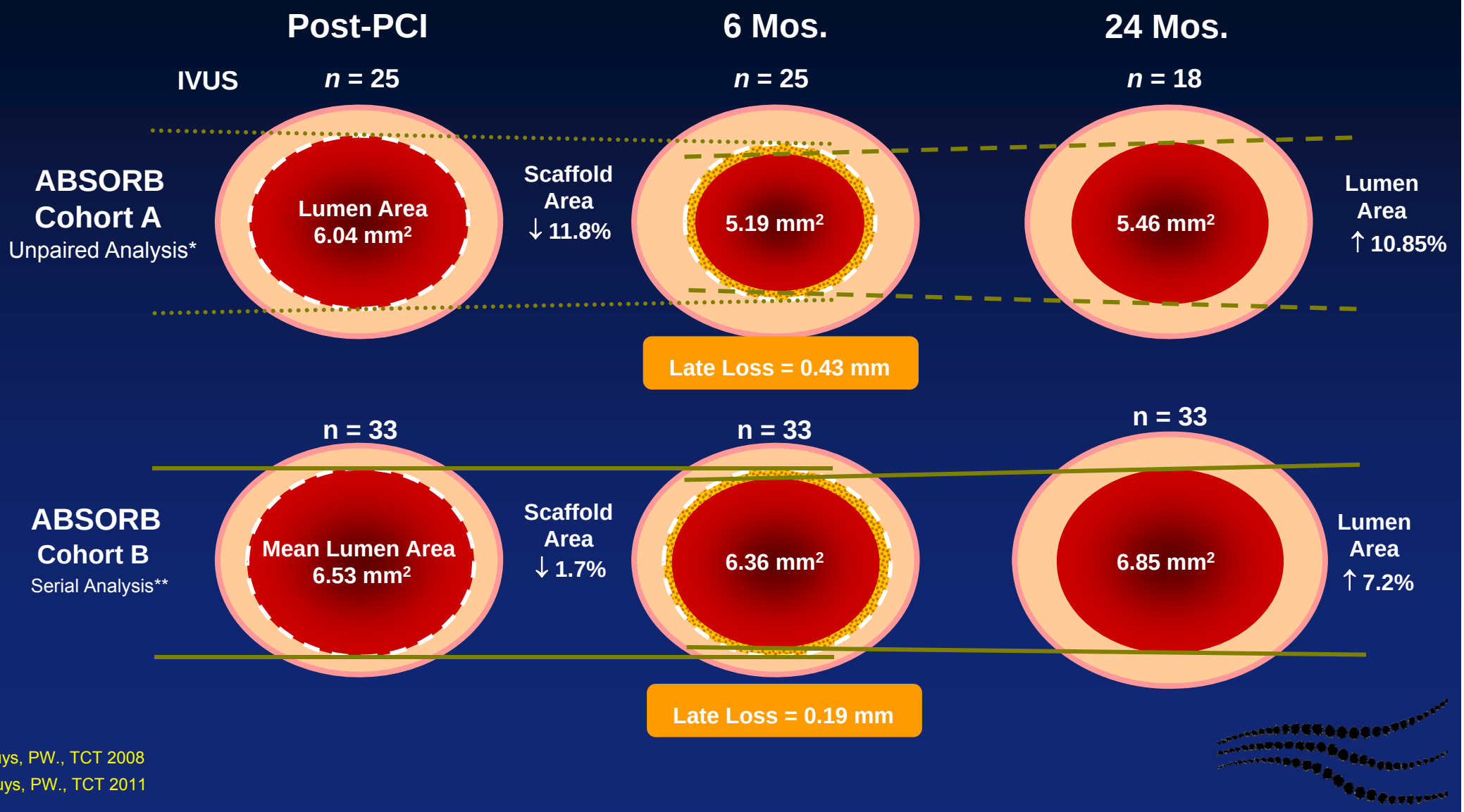
Principal Investigators:

John Ormiston, Patrick Serruys

- **Prospective, open label, single arm study**
- **101 patients enrolled at 12 sites**
- **Device sizes: 3.0 x 18 mm**
- **Treatment: up to 2 *de novo* lesion**
- **Follow-up schedule:**



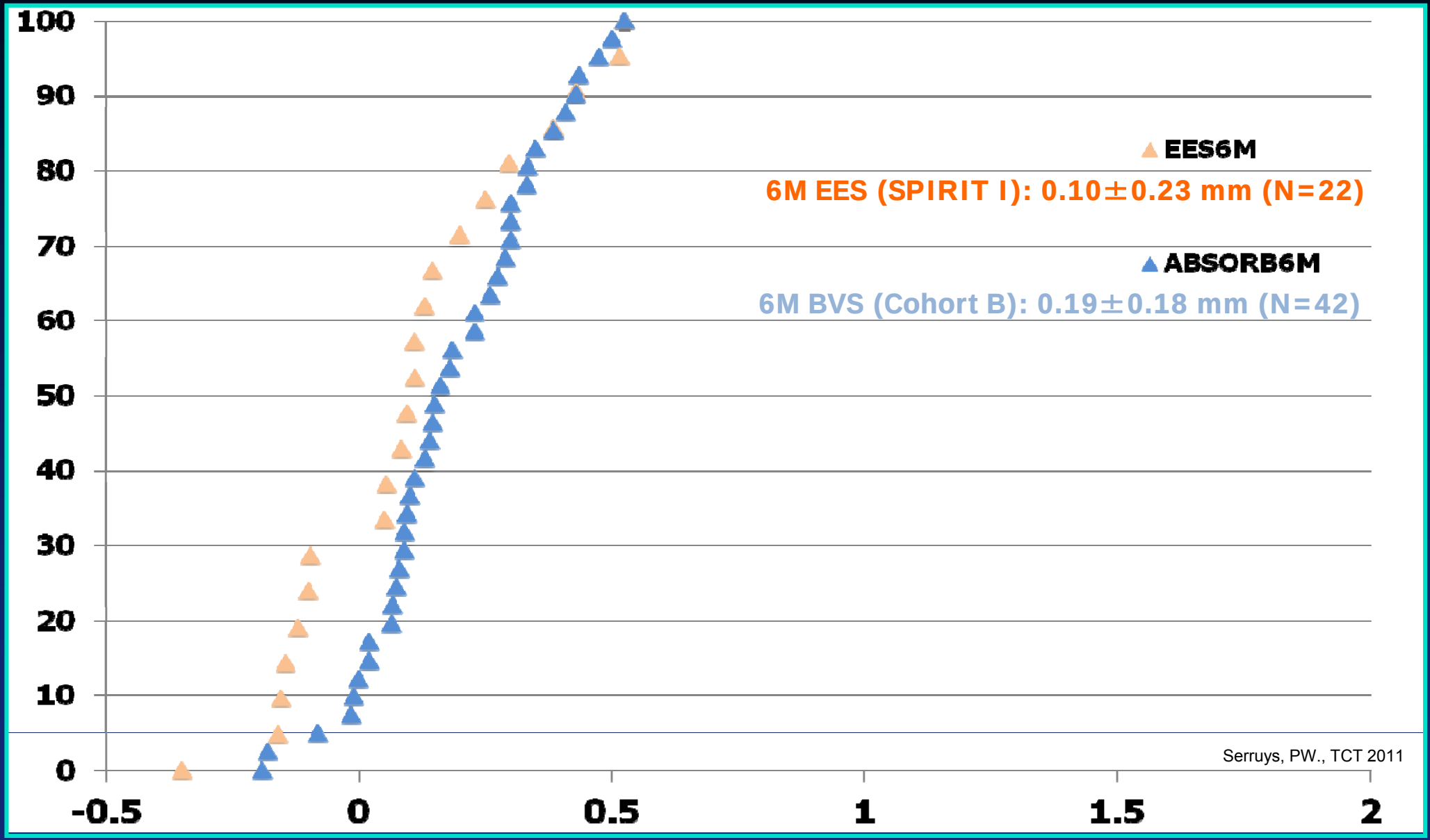
ABSORB Cohorts A and B: Temporal Changes in Lumen Dimensions



*Serruys, PW., TCT 2008

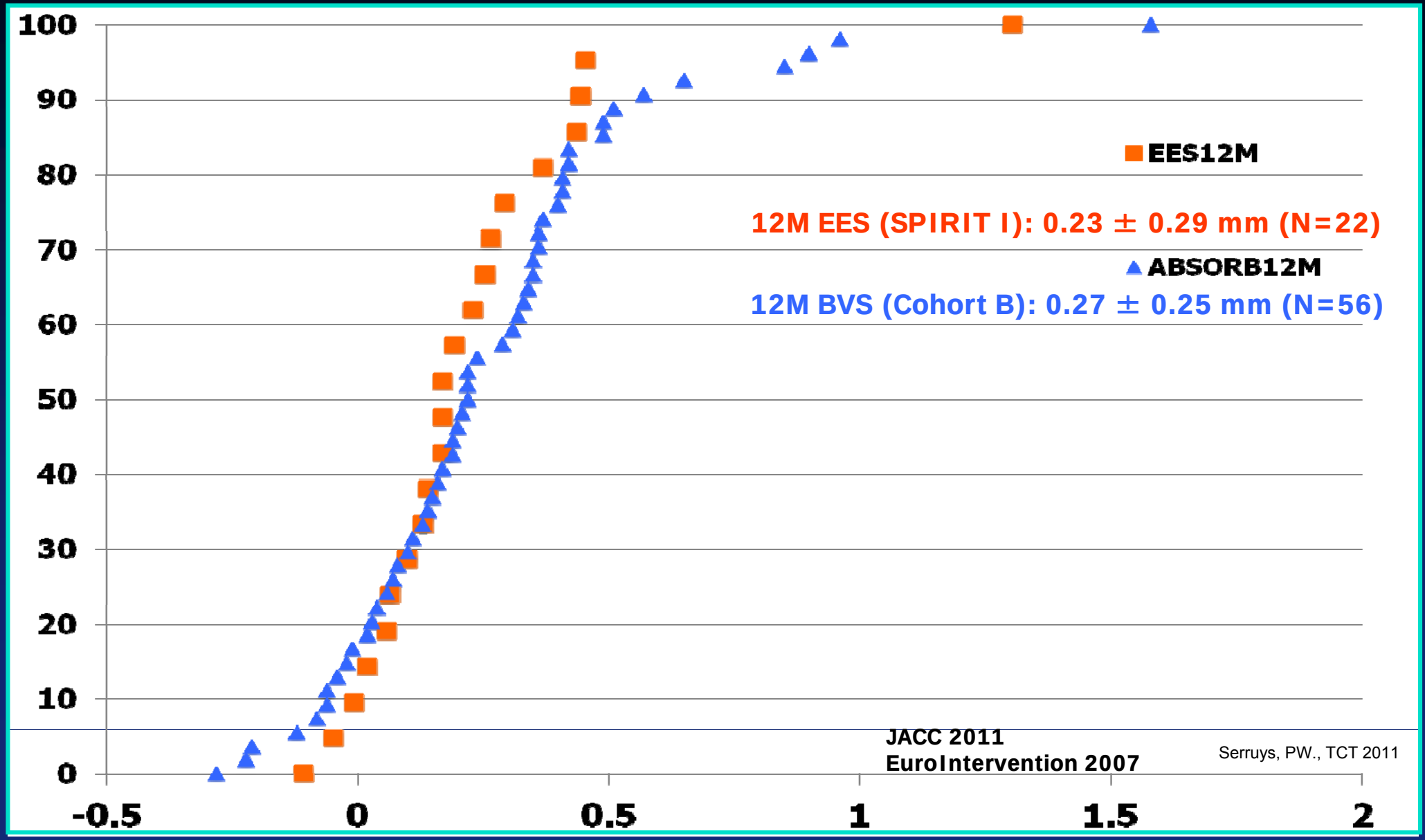
**Serruys, PW., TCT 2011

Evolution of LL Cumulative Curves – 6 Months
ABSORB BVS vs. XIENCE V (non-matched population)



ABSORB BVS is neither approved nor available for sale in the U.S.

Evolution of LL Cumulative Curves – 12 Months
ABSORB BVS vs. XIENCE V (non-matched population)



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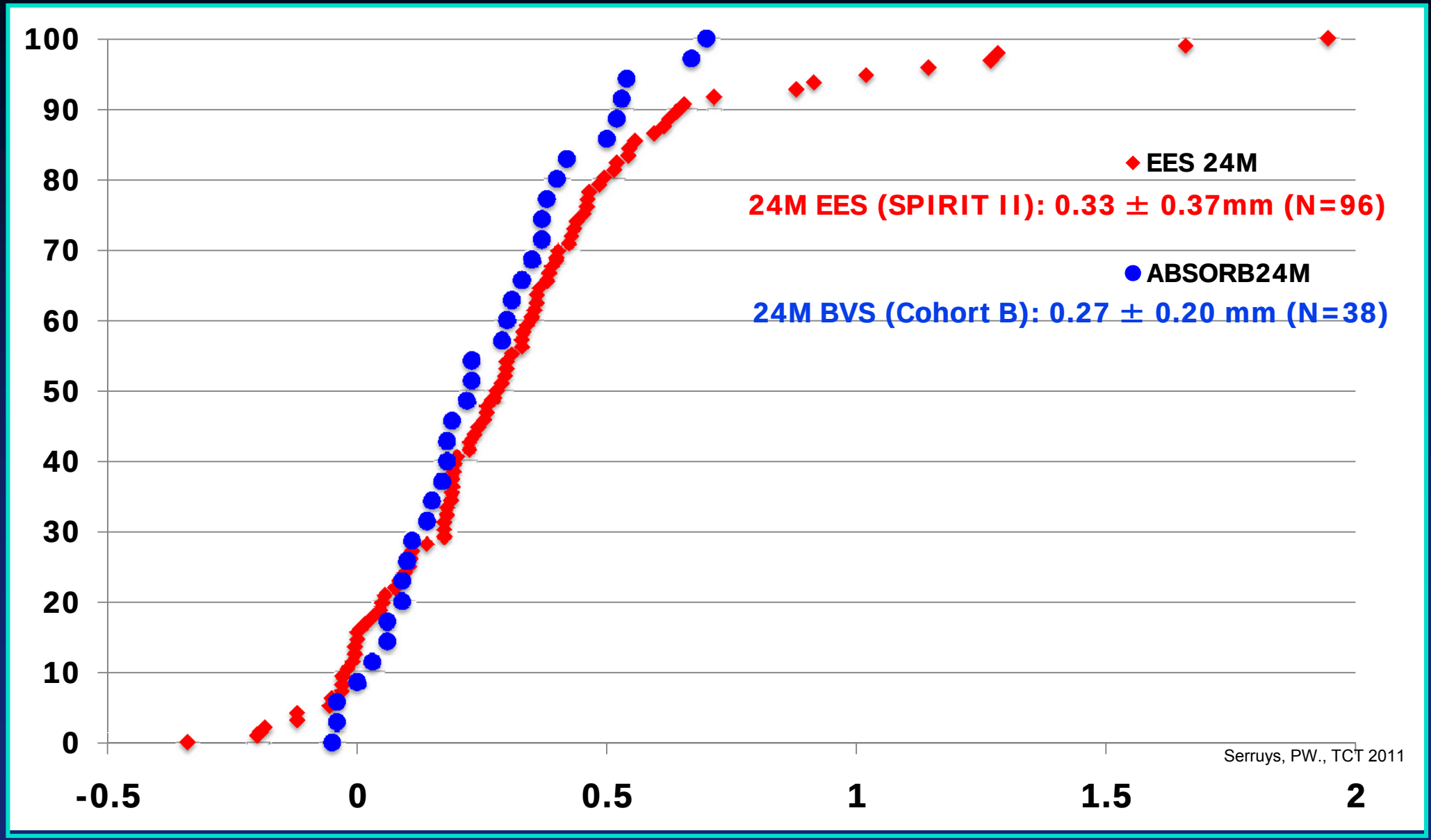
Evolution of LL Cumulative Curves – 24 Months
ABSORB BVS vs. XIENCE V (non-matched population)



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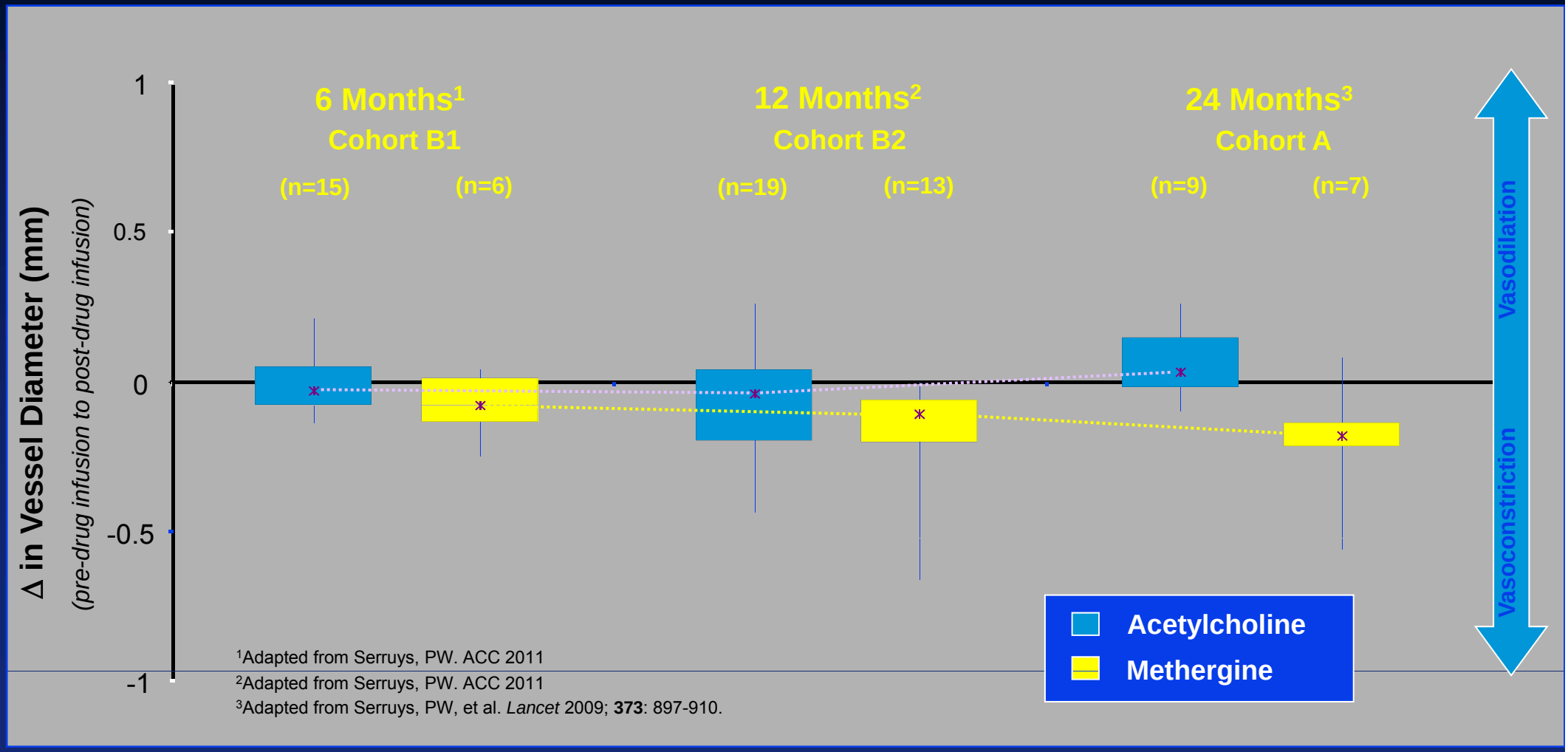
Return of Vasomotor Function



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

ABSORB Cohort B1
Clinical Results up to 2 Years

Non-Hierarchical	1 Year N=45	2 Years N = 44*
Cardiac Death %	**0**	**0**
Myocardial Infarction % (n)	**2.2 (1)**	**2.3 (1)**
Q-wave MI	**0**	**0**
Non Q-wave MI	**2.2 (1)**	**2.3 (1)**
Ischemia driven TLR %	**4.4 (2)**	**4.5 (2)**
CABG	**0**	**0**
PCI	**4.4 (2)**	**4.5 (2)**
Hierarchical MACE % (n)	**6.7 (3)**	**6.8 (3)**

No scaffold thrombosis by ARC or Protocol

*1 patient missed the 2-year visit
MACE: Cardiac death, MI, ischemia-driven TLR

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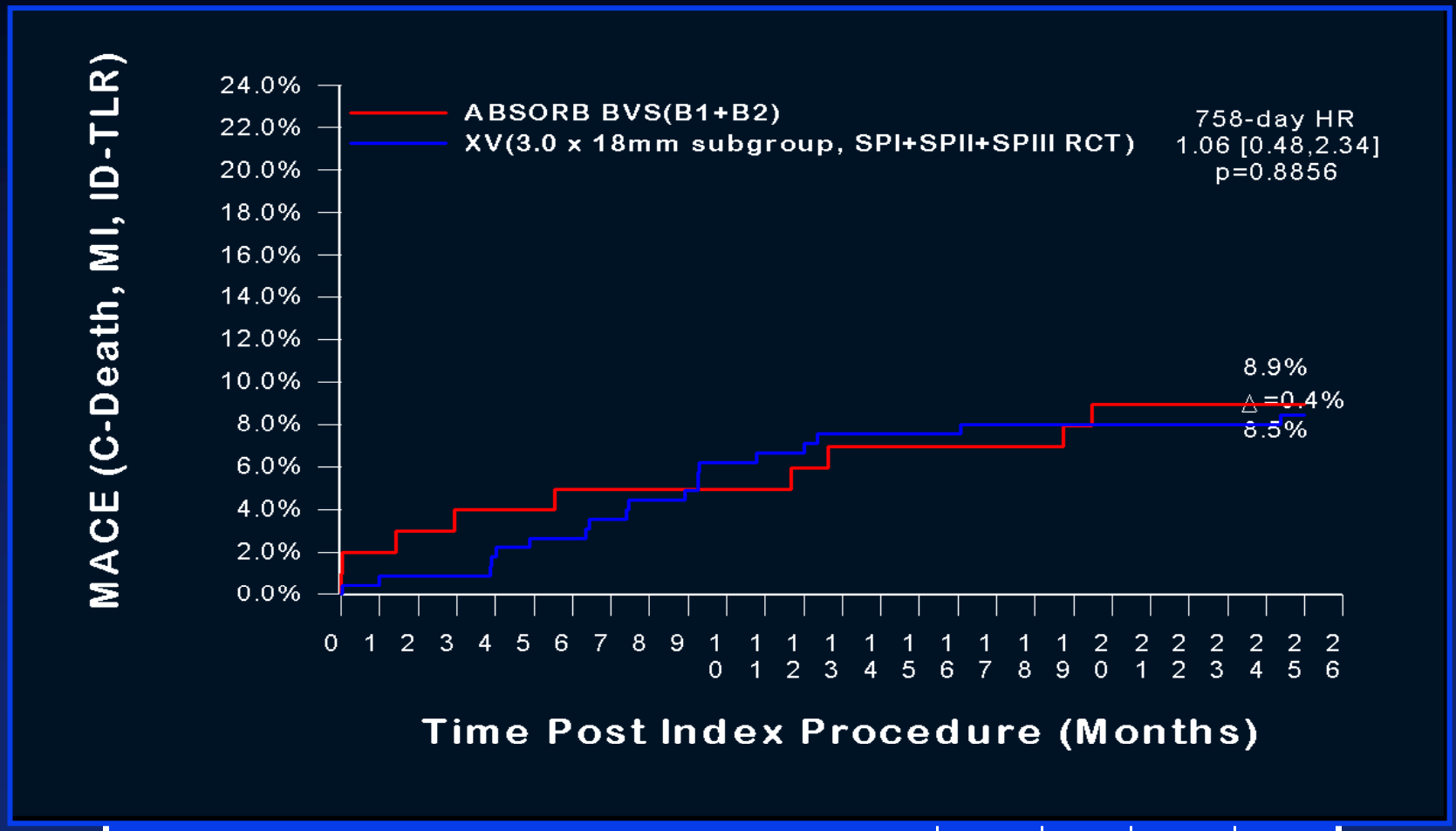
No scaffold thrombosis by ARC or Protocol

*1 patient missed the 2-year visit
MACE: Cardiac death, MI, ischemia-driven TLR

ABSORB Cohort B
MACE Rate Compared to XIENCE V



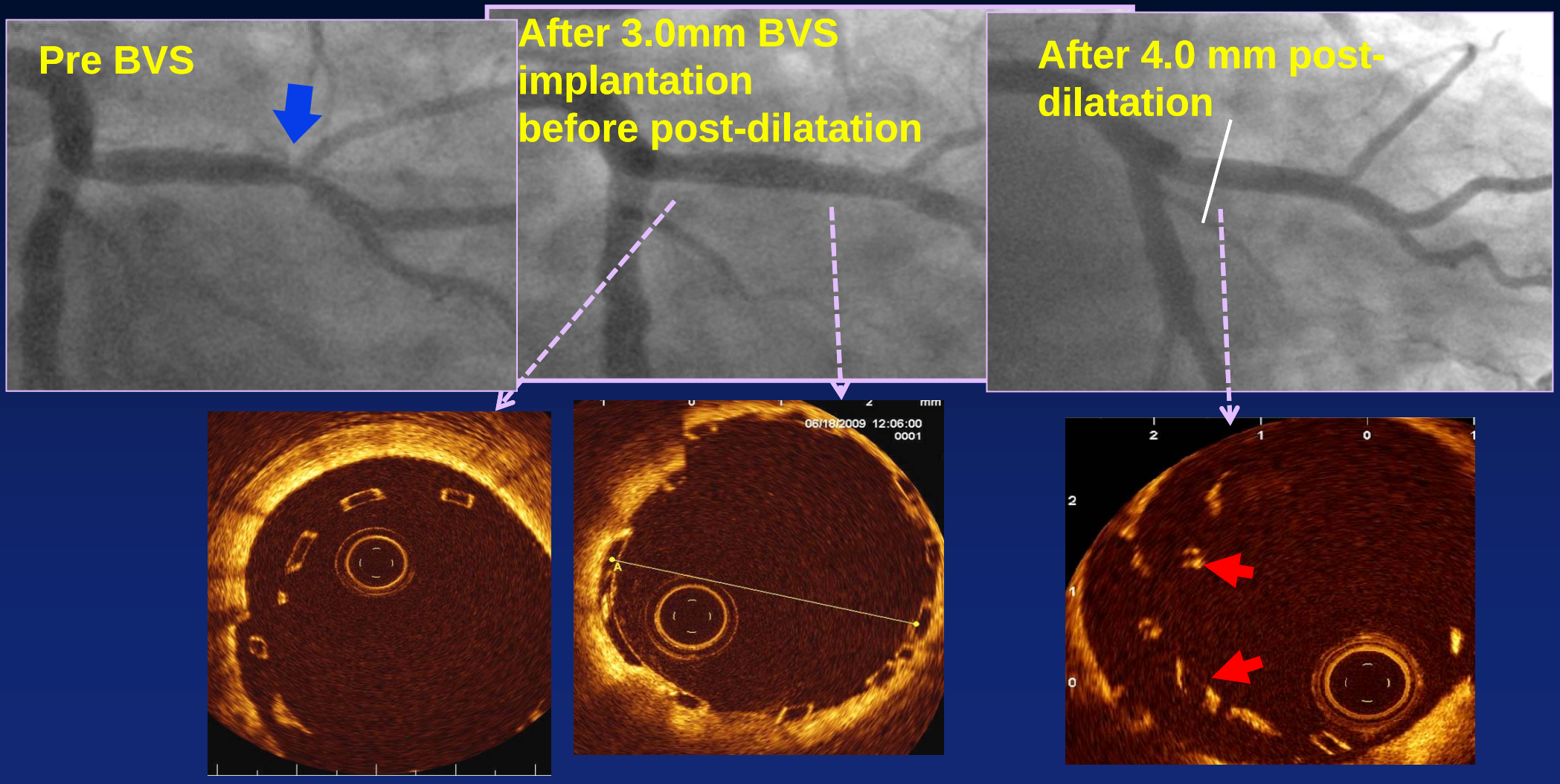
	0	194	393	758
ABSORB BVS(B1+B2) At Risk	101	96	94	91
XV(3.0 x 18mm subgroup, SPI+SPII+SPIII RCT) At Risk	227	219	204	191

ABSORB Cohort B, (n=101) vs. patients treated with a single 3x 18 mm XIENCE V (SPIRIT First+II+III, n=227)

ABSORB BVS is neither approved nor available for sale in the U.S.

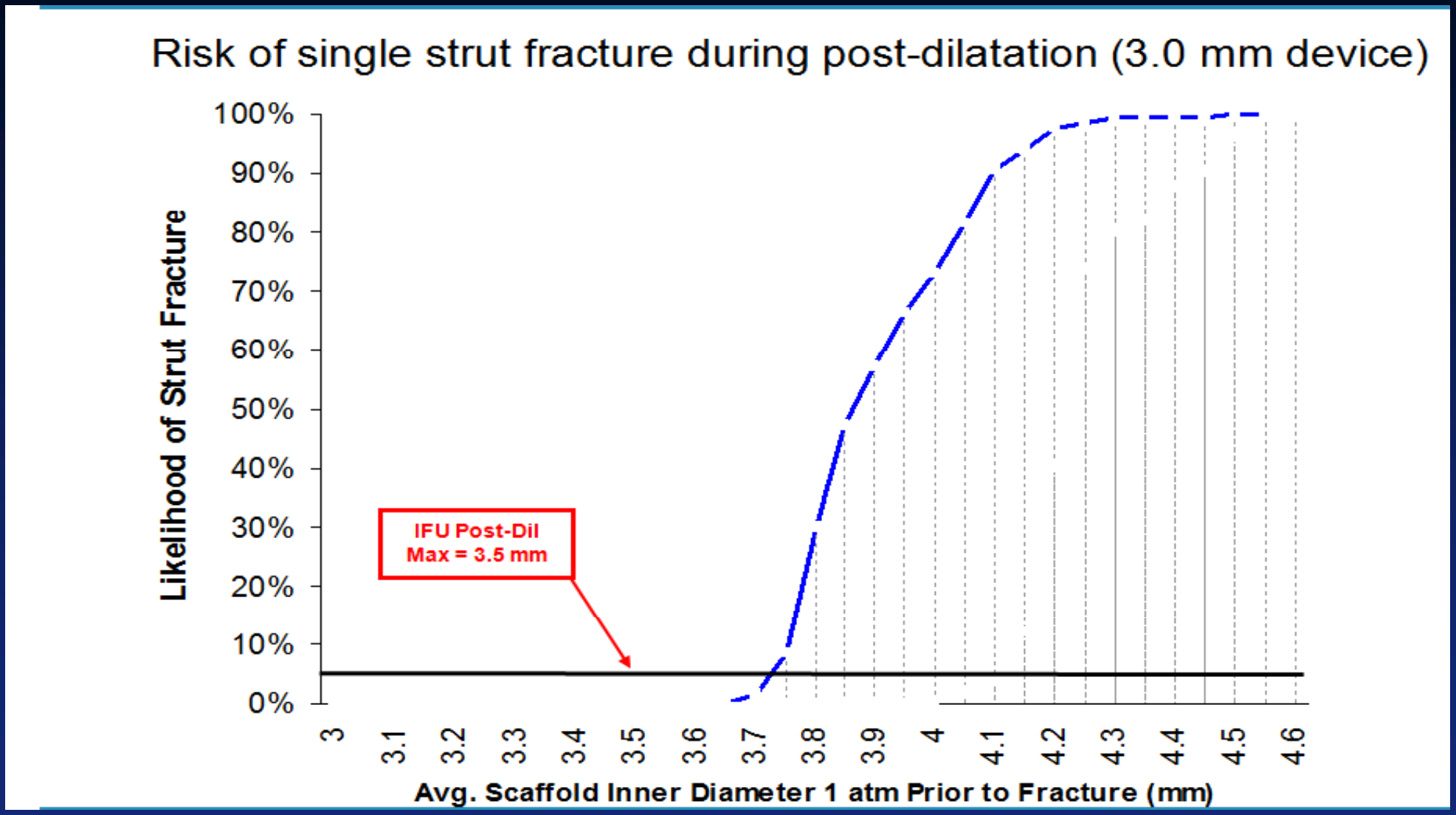
Dudek. ACC 2012

Importance of Accurate Vessel Sizing: ABSORB Cohort B Case Study



Ormiston Circ Interv 2011

Probability of Single Strut Abnormality

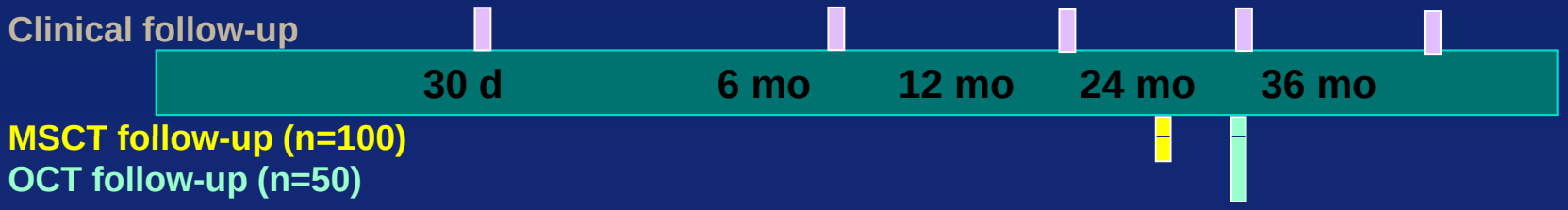


ABSORB EXTEND

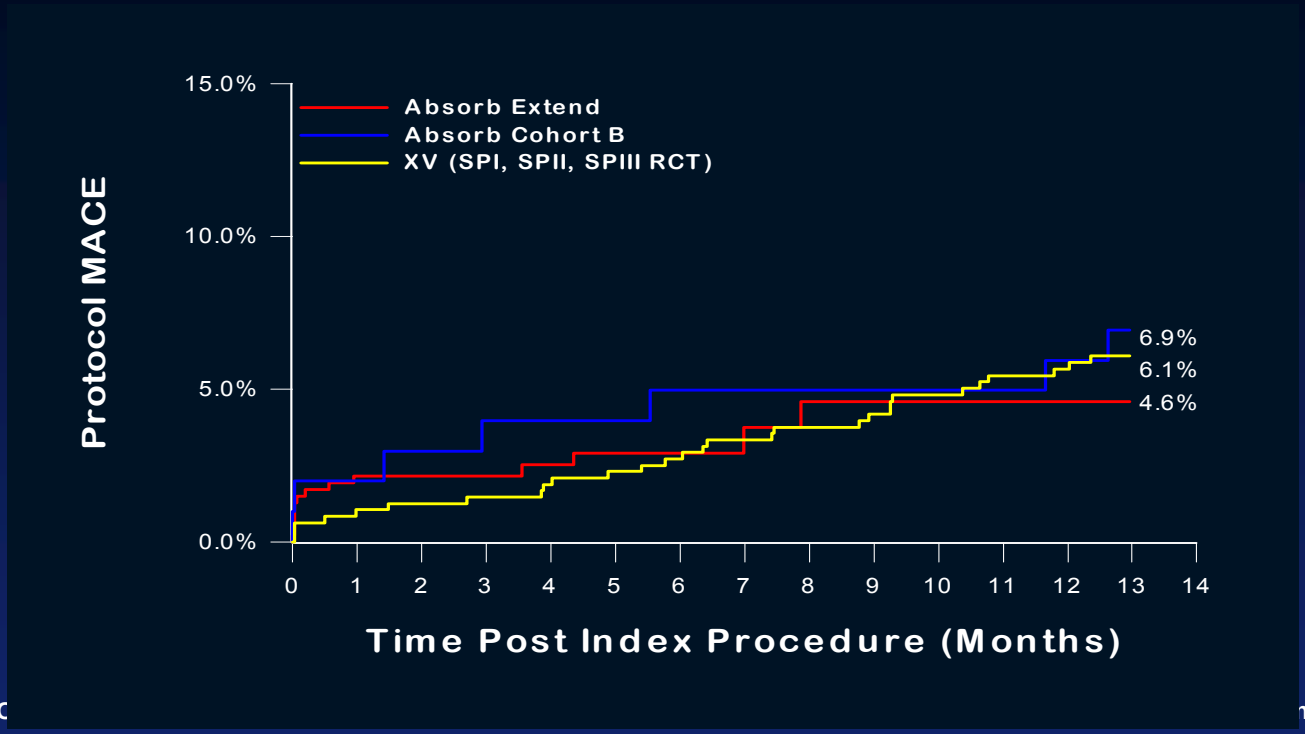
Principal Investigator: Alexandre Abizaid

Co-PI: Antonio Bartorelli; Rob Whitbourn

- Continued Access trial. FPI*: Jan 11, 2010
- No hypothesis-testing, typical PCI endpoints, 1000 patients
- Device Sizes: 2.5, 3.0 mm (diameters); 18, 28 mm (lengths)
- Lesion lengths ≤ 28 mm
- Planned overlap allowed
- Two imaging subgroups: OCT (n=50, planned overlap only); MSCT (n=100)
- Follow-up schedule:



ABSORB EXTEND vs Cohort B vs SPIRIT Pooled (SPIRIT I + II + III):*
Protocol MACE K-M curves up to 12 Months



Note: ABSC n.

Days After Index Procedure	0	37	194	393
BVS EXTEND at Risk	469	440	260	112
ABSORB Cohort B at Risk	101	99	96	94
SPIRIT Pooled at Risk	482	475	462	435

Note: Due to the interim nature of this analysis, FU data is not available for every subject at every timepoint.
*SPIRIT Pooled is defined as those subjects receiving either a 3.0 x 18 mm, 2.5 x 18 mm, or 3.0 x 28 mm XIENCE V stent from the SPIRIT FIRST + SPIRIT II + SPIRIT III trial populations.

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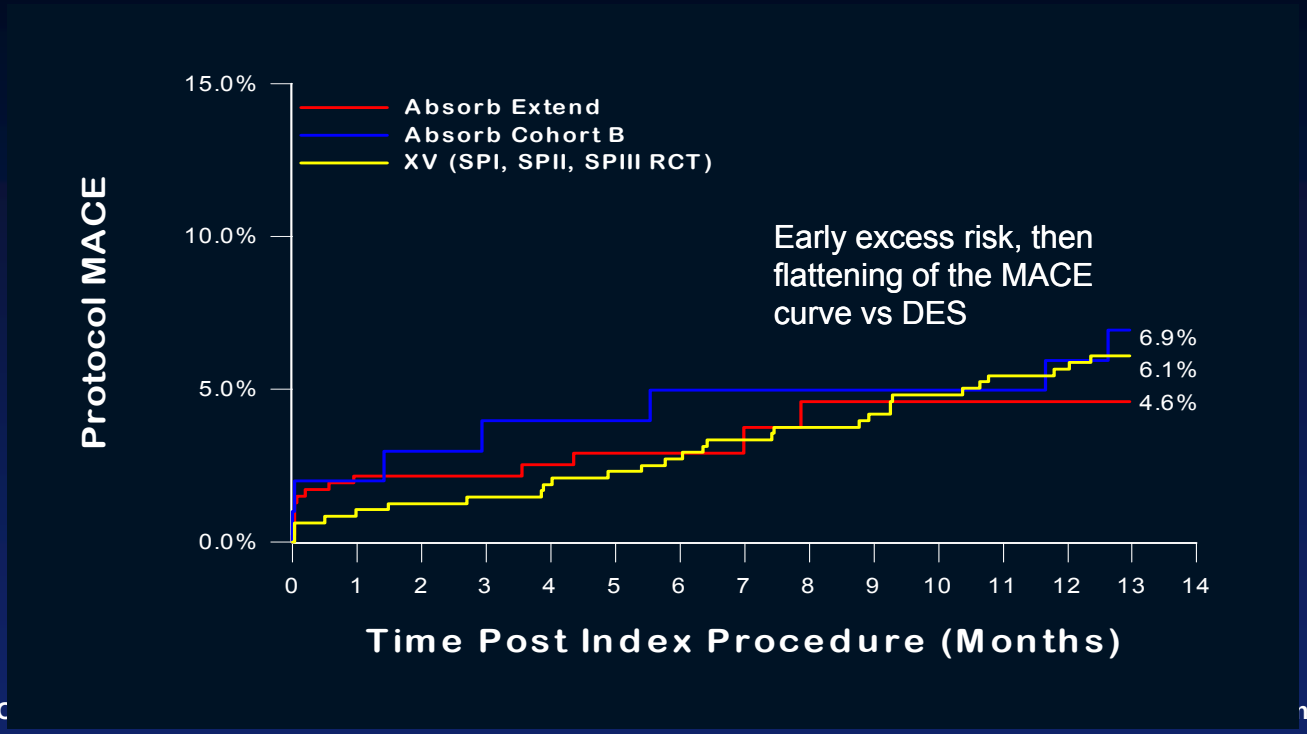

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ABSORB-RCT

ABSORB III (N~2300)

PI: Steve Ellis, Dean Kereiakes

Objective: For US approval of BVS

Primary Endpoint: Target Lesion Failure (TLF) at 1 year non-inferiority to XIENCE V/PRIME

ABSORB IV (N~3000)

PI: Gregg Stone

Co-PI: Steve Ellis, Dean Kereiakes

Objective: For label claims

Major Sec. Endpoint: Landmark analysis on TLF from 1 to 5 years, superiority to XIENCE V/PRIME

ABSORB-U.S. RCT

Some Key Issues Still Under Discussion

1) What is the proper definition of peri-procedural MI (drives sample size)?
2) How should predilatation strategy be prescribed and if different than usual, when should patient be randomized?
3) Given U.S. practice of not usually using QCA for vessel sizing, what strategy/training is needed to assure proper BVS sizing?

ABSORB-U.S. RCT

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To Start Approximately December 2012!