The ABSORB Program

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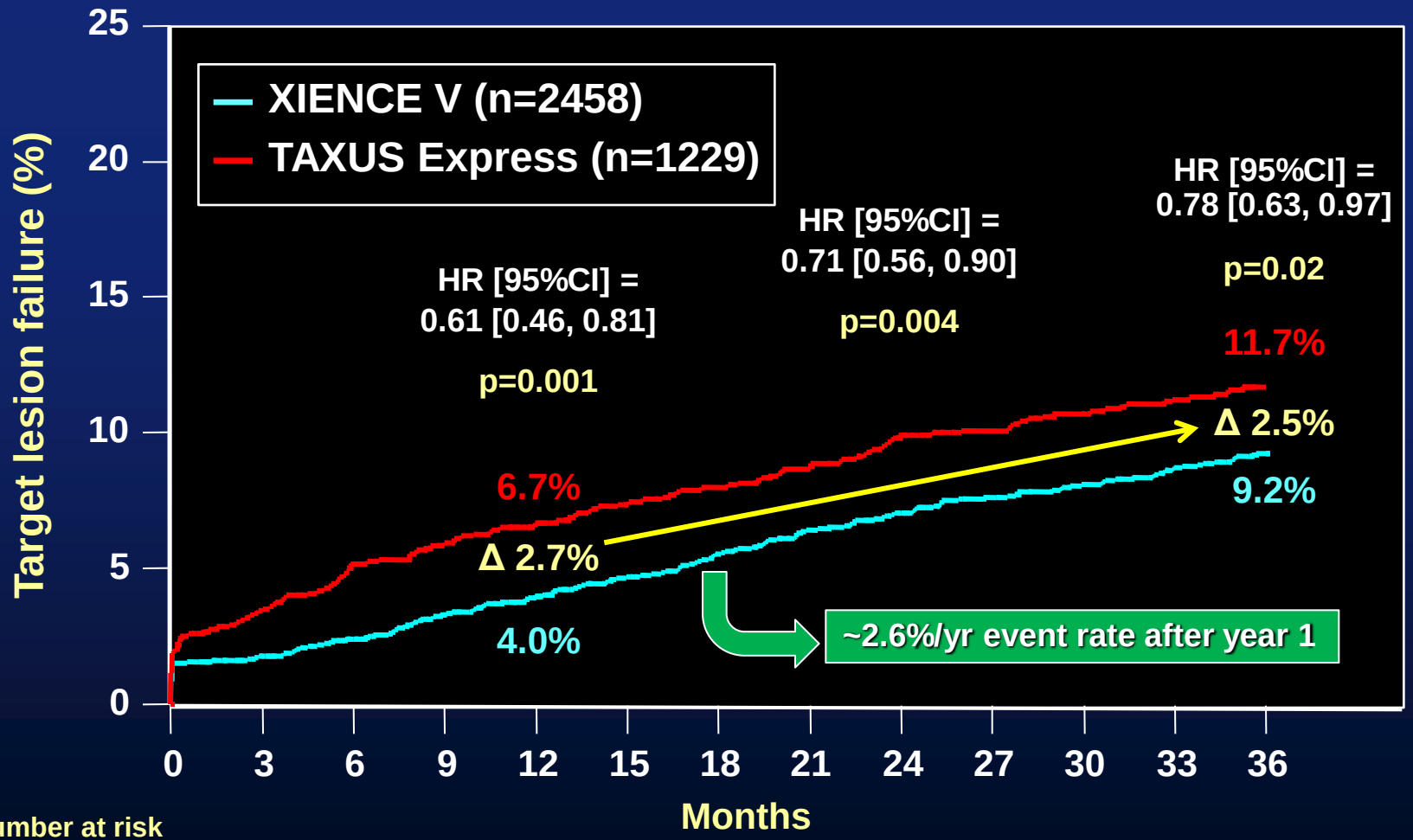
TCT-AP 2014

Rationale for BRS: SPIRIT IV: TLF @3 Years



Number at risk

XIENCE V	2458	2390	2364	2323	2281	2238	2212	2187	2162	2132	2116	2095	2074
TAXUS	1229	1166	1138	1119	1095	1069	1060	1049	1029	1019	1008	994	979

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

Stone GW et al. JACC 2011 (abstract)

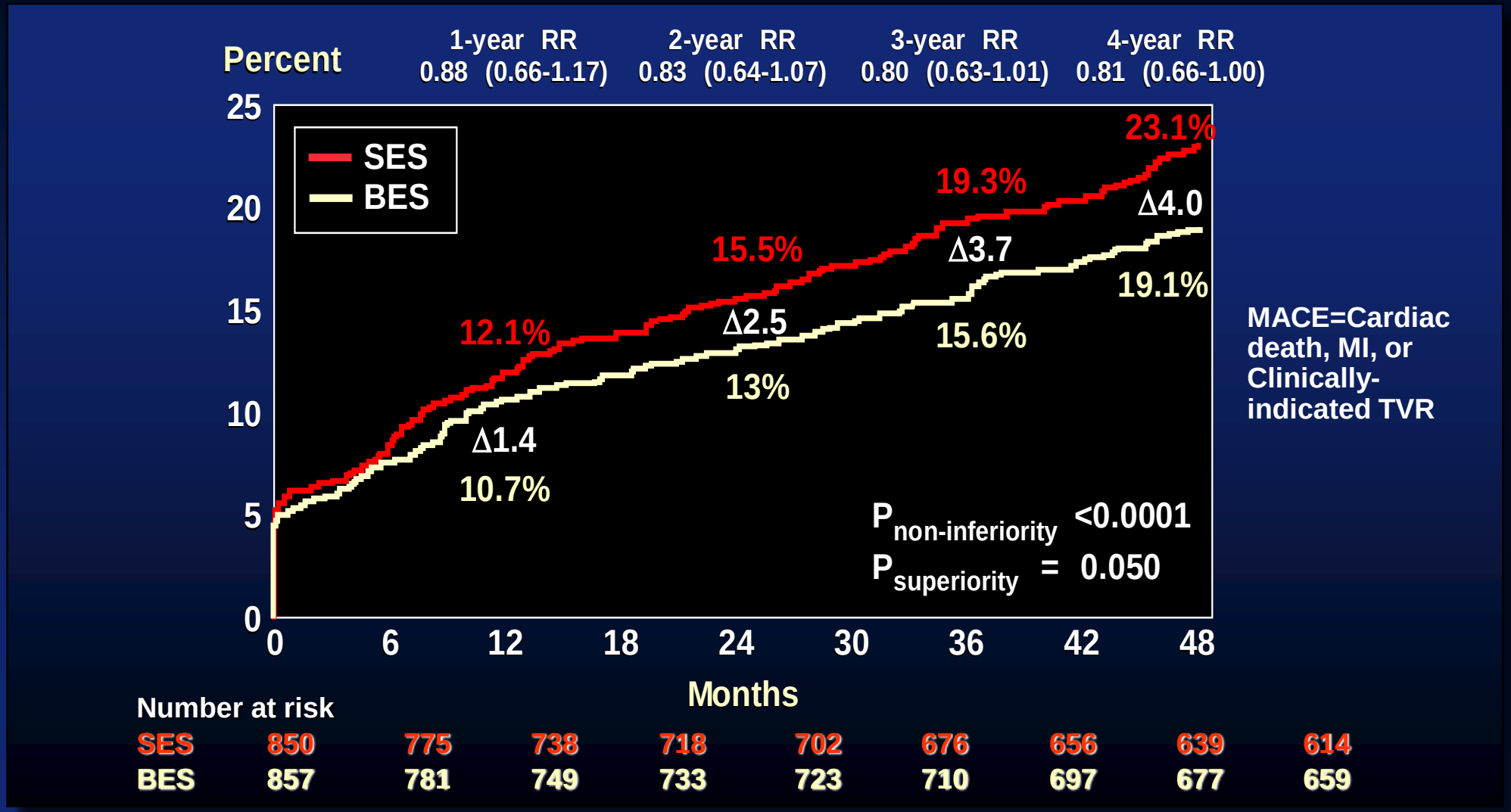
Why Might BRS Reduce Late TVF?

Possible DES Concerns: The Polymer/The Metal Stent

- Less neointimal-based restenosis
- Less neoatherosclerosis
- Less vasospasm
- More late lumen enlargement (vessel enlargement/plaque regression)
- More responsive to physiologic stimuli

Biodegradable vs Biostable Polymer-Based DES

LEADERS: Long Term MACE



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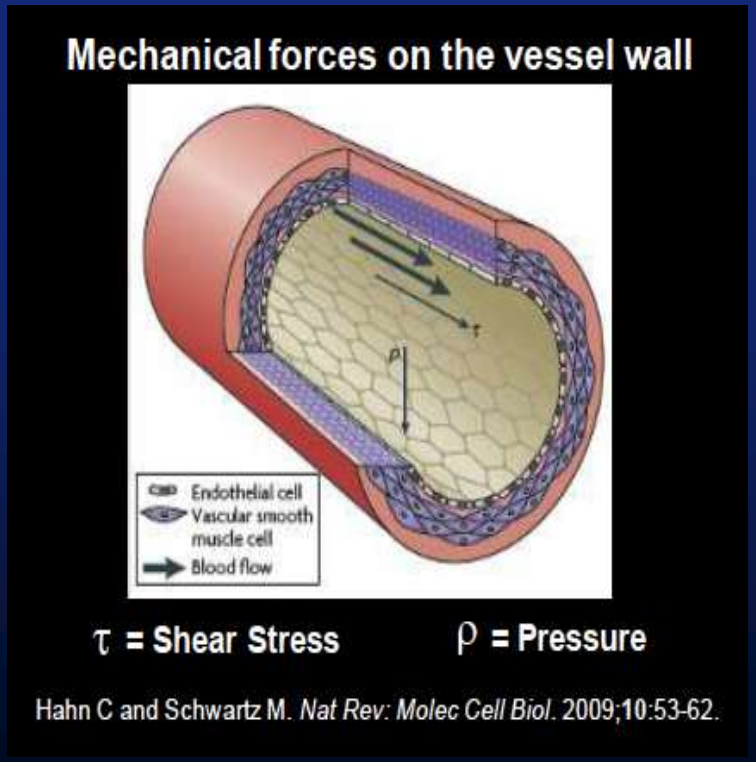
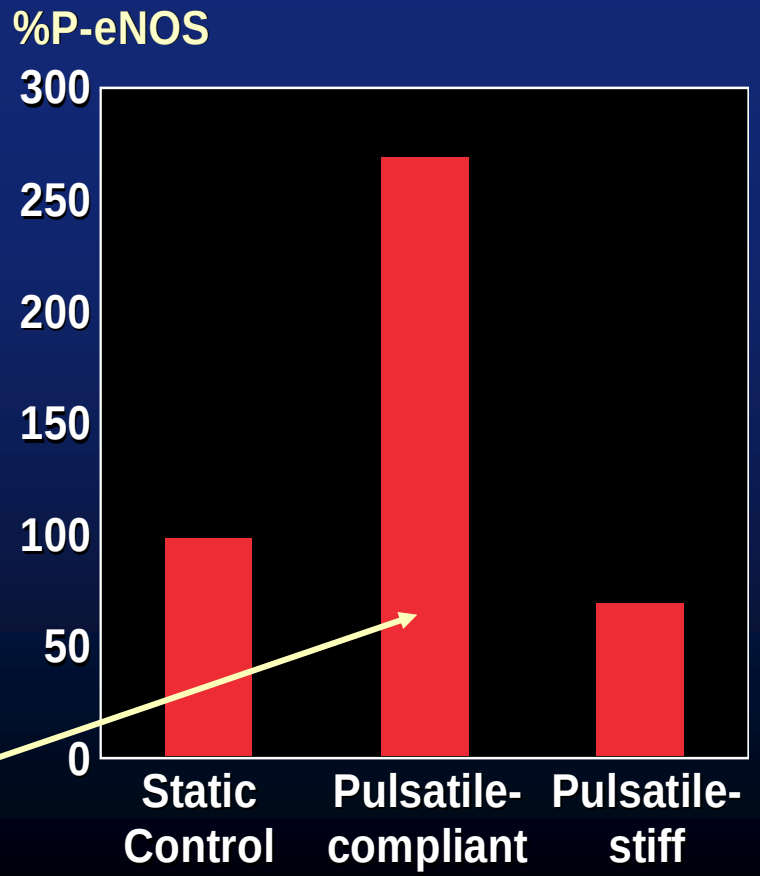
SGE; 0414-6, 3

Impact of Physiological Cyclic Strain and Shear Stress on Vessel Wall Biology

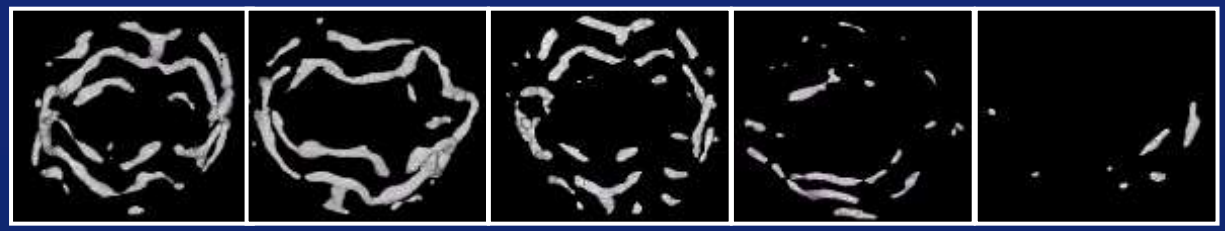
The Translation Of Mechanical Forces Into Chemical Signals By Cells Is Referred To As "Mechanotransduction"

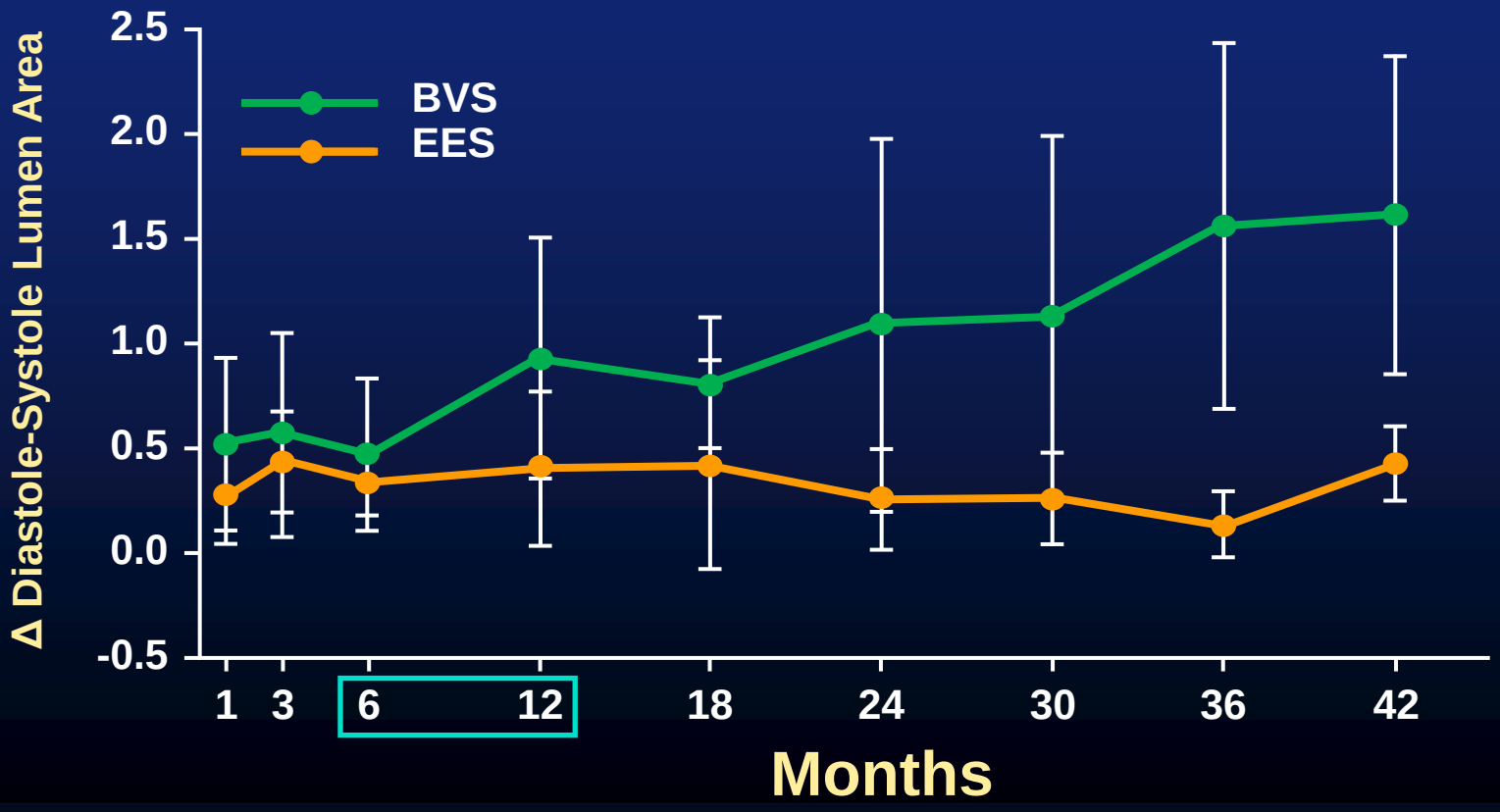


Normal responses to physiologic pulsatile cyclic strain and shear stress lead to cellular responses that stabilize the vessel



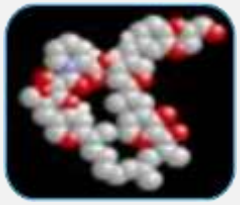
BVS: Restoration of Pulsatility in the Porcine Coronary Model

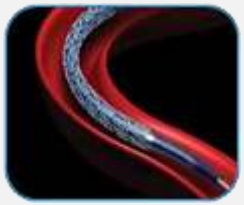




Data on file, Abbott Vascular

BVS Design Elements
Built on XIENCE Safety Profile





	DRUG/ DOSE	RELEASE RATE / COATING	STENT DELIVERY SYSTEM	STENT DESIGN	STENT MATERIAL
XIENCE V	Everolimus 100 µg/cm^2	80% in 28d 100% in 3 months Fluoro-Polymer	Multi-Link VISION	Multi-Link Family	Cobalt Chromium
BVS	Everolimus 100 µg/cm^2	80% in 28d 100% in 3 months PDLLA	Multi-Link VISION	Multi-Link Family	PLLA

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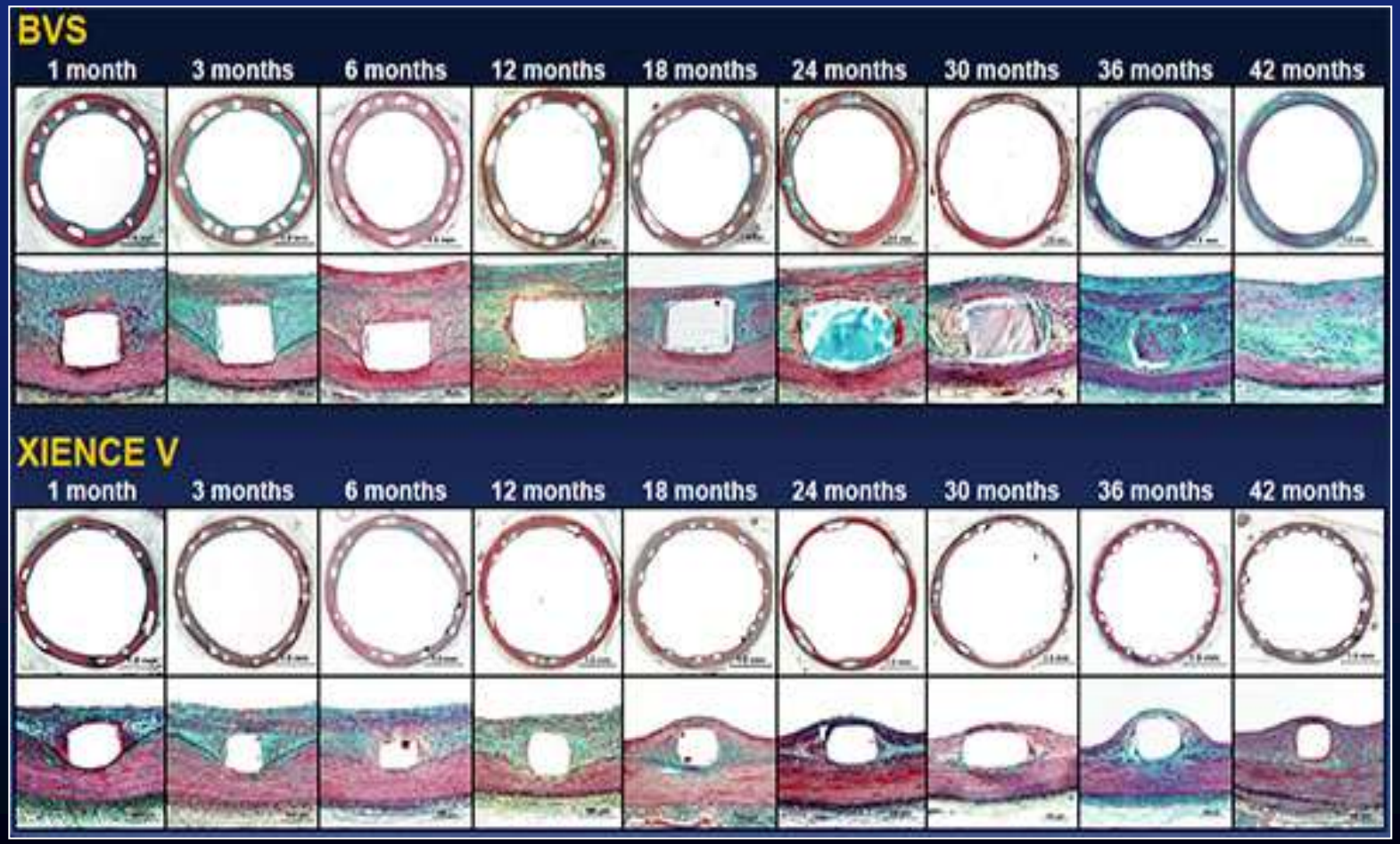
Representative Histologic Images of BVS and XIENCE V in Porcine Coronary Arteries from 1 to 42 Months

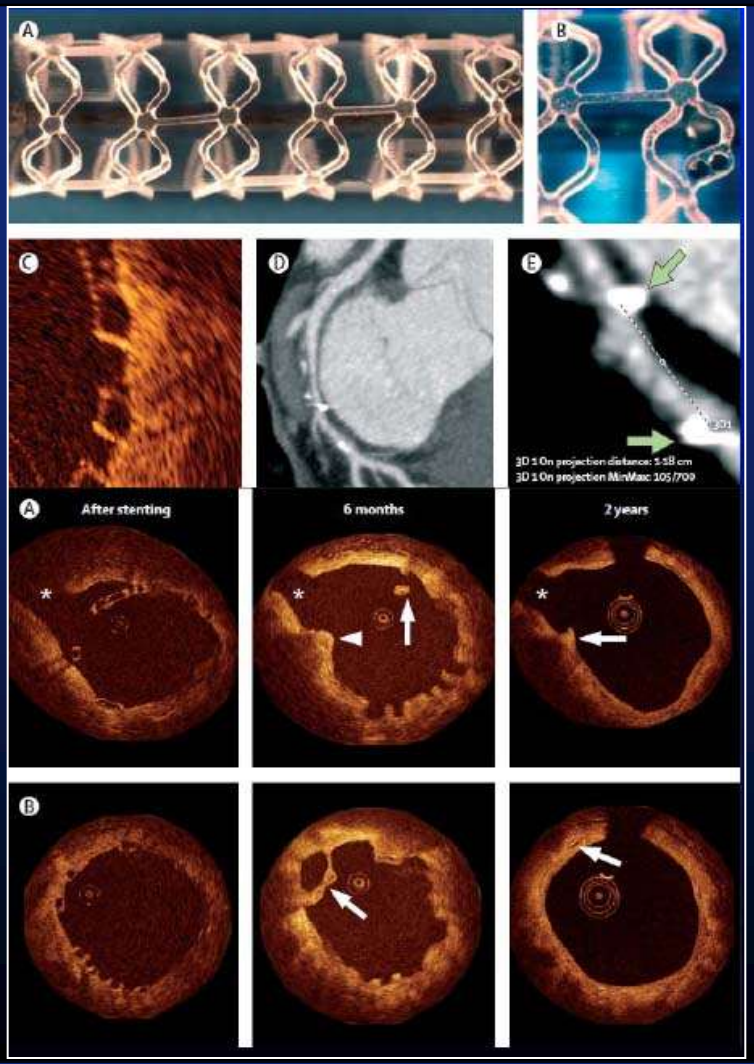


Otsuka, Virmani, et al., CV Path Institute Institute, Inc

SGE; 0414-6, 6

BVS: A Fully Bioabsorbable Everolimus - Eluting Stent

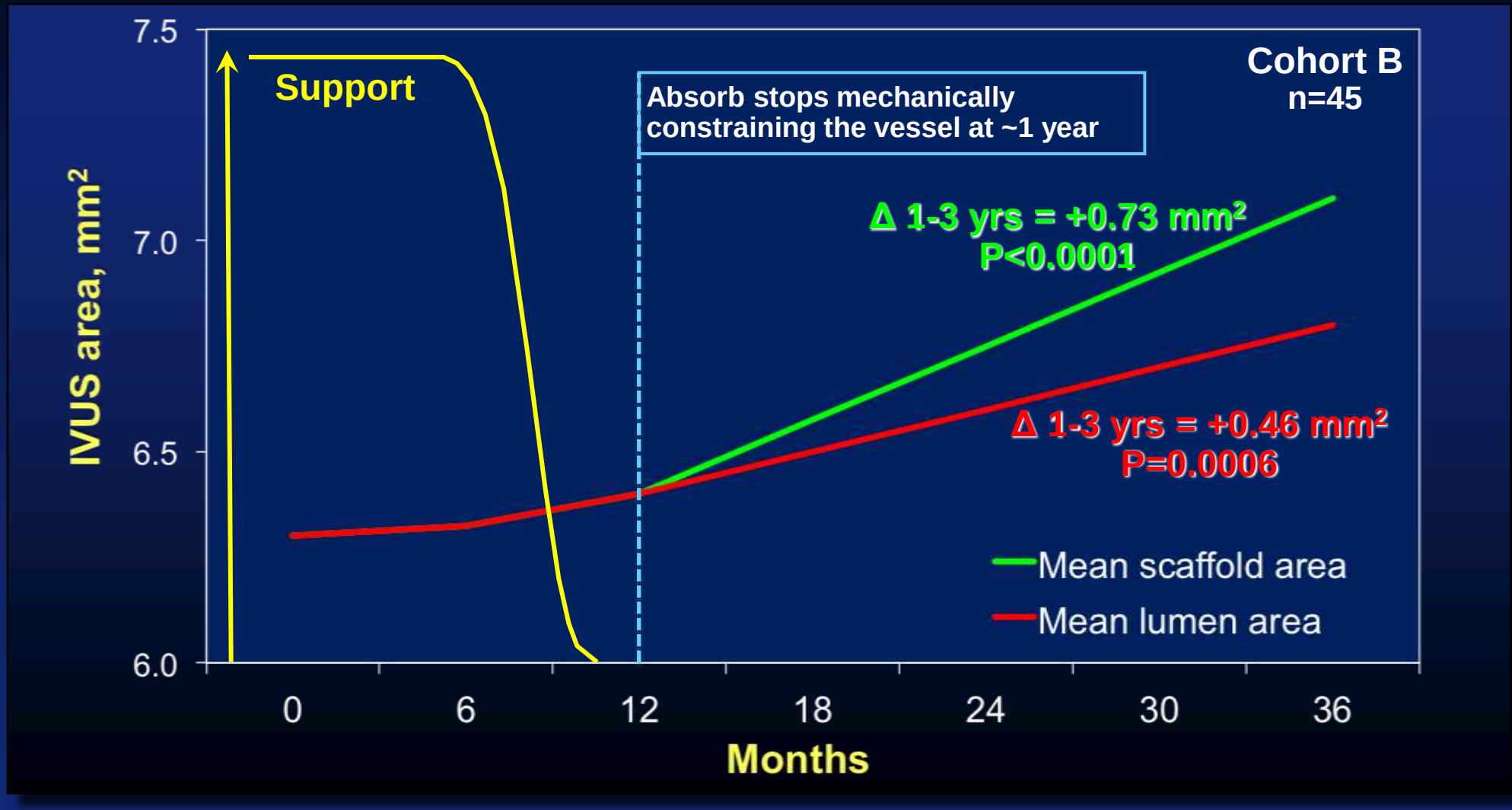
Thin coating everolimus/PLLA matrix
for controlled drug release
PLLA stent backbone for stent integrity



Serruys PW et al. Lancet 2009;373:897 Onuma Y et al. Circulation 2011;123:779

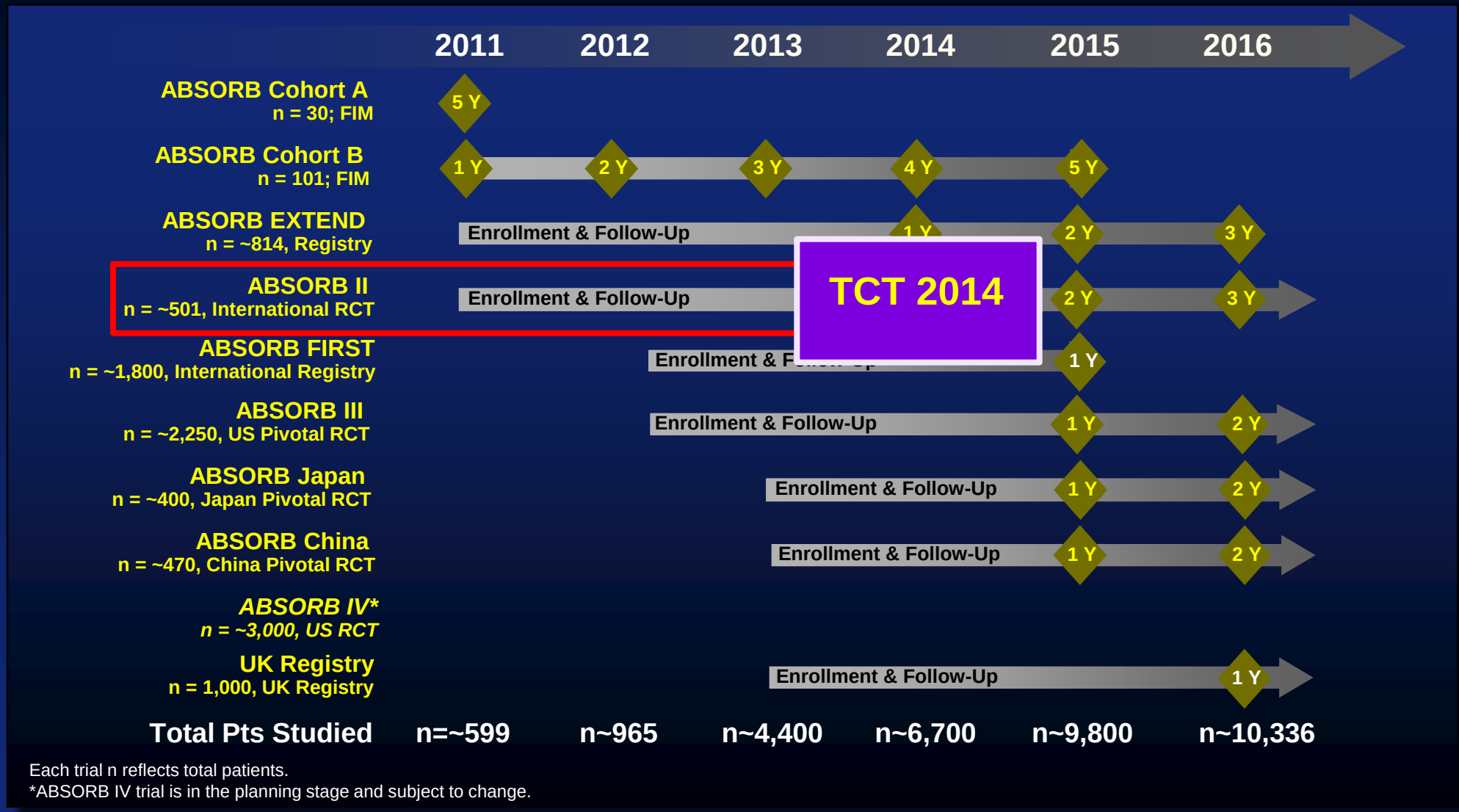
SGE; 1111-5, 16

Potential Paradigm Shift: Late Lumen Gain Offers Potential for Late Post PCI MACE/Angina Decrease



Cohort B 3-year data Serruys PW. ACC 2013

ABSORB: Comprehensive Abbott Vascular - Sponsored Clinical Trial Program



Each trial n reflects total patients.
*ABSORB IV trial is in the planning stage and subject to change.

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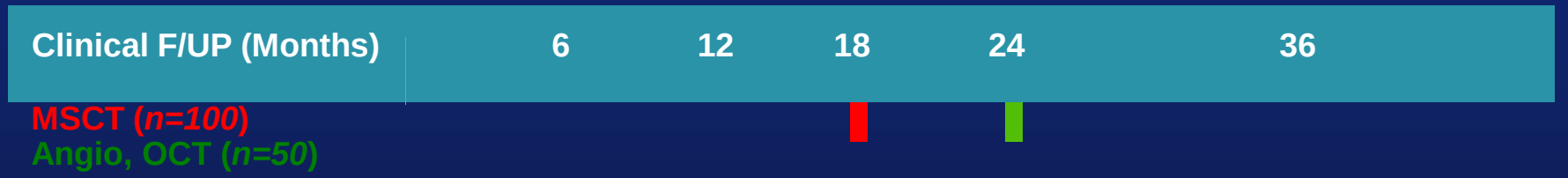
SGE; 0414-6, 7

ABSORB EXTEND

~800 subjects

Non-randomized, single arm trial, 57 sites in Europe, APJ, Brazil, Canada

PI: Alex Abizaid; Regional PI: Antonio Bartorelli, Robert Whitbourn

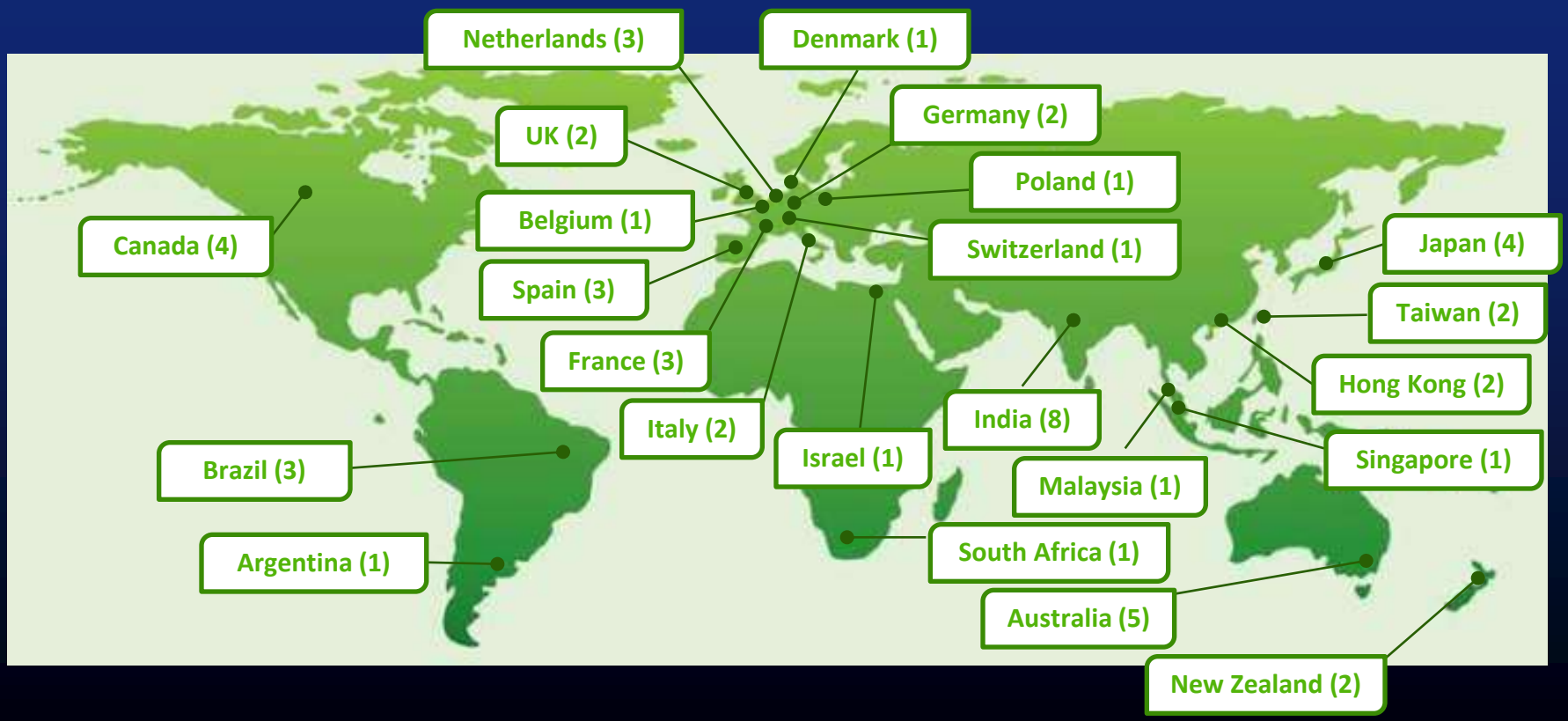


Study Objective	Continued Access trial. FPI: Jan 11, 2010
Endpoints	Typical PCI clinical endpoints
Treatment	Up to 2 *de novo* lesions in different epicardial vessels Planned overlapping allowed in lesions >22 and ≤ 28 mm
Device Sizes	Scaffold diameters: 2.5, 3.0, 3.5 mm Scaffold lengths: 12*, 18, 28 mm

** 2.5 x12 and 3x12 mm to be introduced into the trial once available.*

ABSORB EXTEND - Clinical Sites

Expansion in clinical sites, worldwide



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ABSORB II Randomized Controlled Trial

Prospective, single blind, randomized 2:1 Absorb BVS (334) vs. XIENCE (167)
~501 patients in ~40 sites in EUR and NZ

PI: Patrick Serruys

Co-PI: Bernard Chevalier

Clinical follow-up

Angio, IVUS, CCTA Imaging Fup
(CCTA at 3 years except for GER subjects)
QoL/PRO Tools (★)

Co-Primary Endpoints	1) Change in Mean Lumen Diam. between pre-and post-nitrate at 3 years by QCA (superiority) 2) Change in Minimum Lumen Diam. , Post-procedure to 3 years by QCA (non-inferiority, reflex to superiority)
Powered Secondary Endpoint	1) In-stent/scaffold mean lumen area change from post-procedure to 3 years by IVUS (superiority)

ABSORB III and IV
U.S. Clinical Plan

US ABSORB Program and Trial Strategy

Protocol 10-392

ABSORB III
US Approval Trial, n~2250

Lead-in Cohort (n <=50)	Training	✓ n=24
Primary Cohort, RCT (n~2000)	Approval SDA claim	Enrollment Complete 4/14
Imaging Cohort, RCT RCT (n~200)	Vasomotion, & late lumen growth claims	FPI soon
PK Sub-study (n=12)	Pharmacokinetics	FPI soon

Achieve Approval

SGE; 0414-6, 12

ABSORB III Randomized Controlled Trial

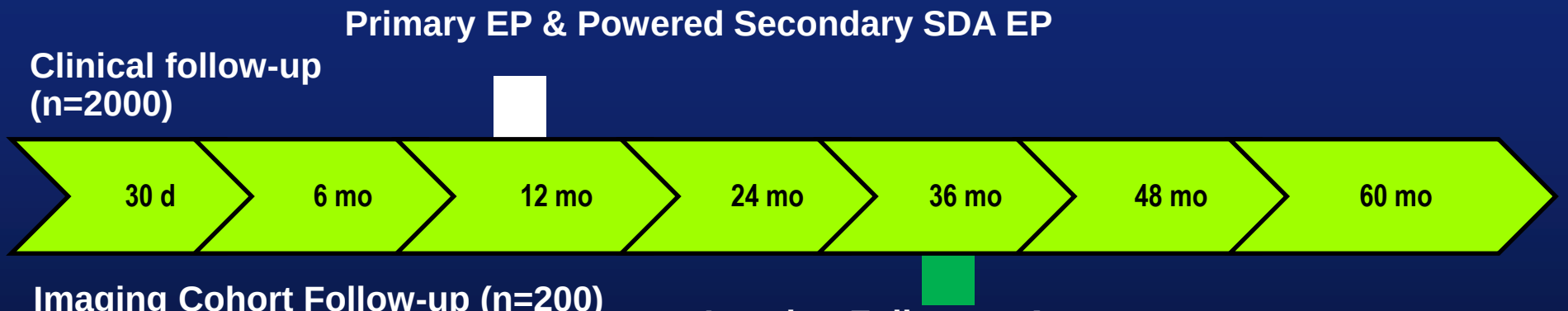
- **Principal Investigators: Dean Kereiakes & Stephen Ellis**
- **Study Chair: Gregg Stone**

Evaluate safety and effectiveness of Absorb BVS in up to two *de novo* lesions in separate epicardial vessels

RVD 2.5 mm – 3.75 mm; Lesion length ≤ 24 mm

ABSORB III Randomized Controlled Trial

Prospective, single blind, randomized 2:1 Absorb BVS vs. XIENCE
Up to 2250 patients in up to 220 US and non-US sites

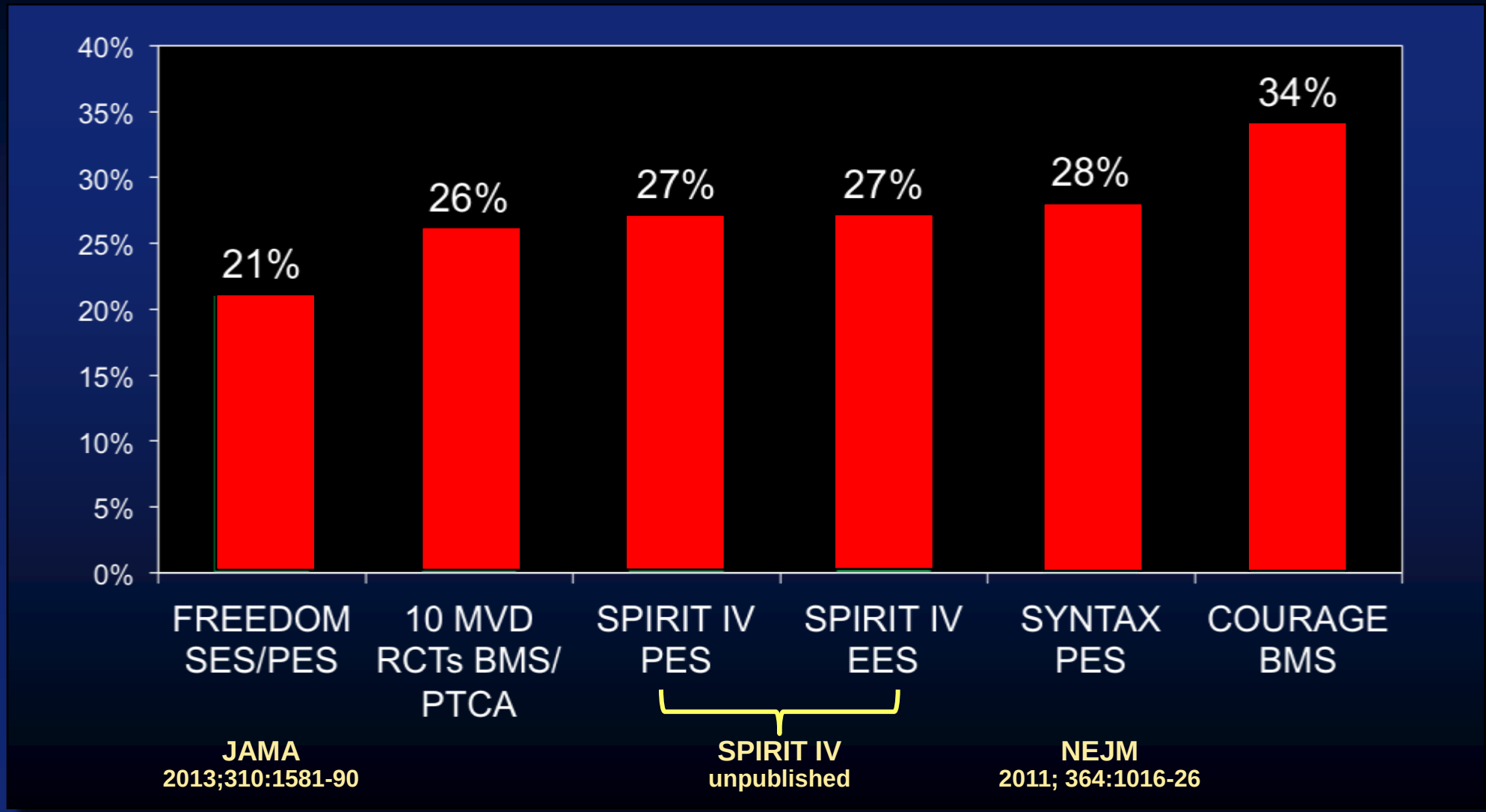


Primary Endpoint	Target lesion failure at 1-year (composite of cardiac death, target vessel MI or clinically indicated TLR), powered for non-inferiority in 2000 clinical follow-up subjects
Powered Secondary Endpoints	1) Site diagnosed angina at 1 year test for superiority of Absorb BVS to XIENCE (n=2000) 2) Nitrate-induced vasomotion at 3 years by QCA 3) Mean lumen area change from baseline to 3 years by IVUS 4) Quality of life/Patient reported outcomes

Post-PCI Angina: Origin of Interest with ABSORB

- Antonio Colombo (2013) “I think my ABSORB patients are having less angina”
- Led to examination of XIENCE RCT and ABSORB registries that collected site diagnosed angina as an endpoint

Angina at 1 Year After PCI



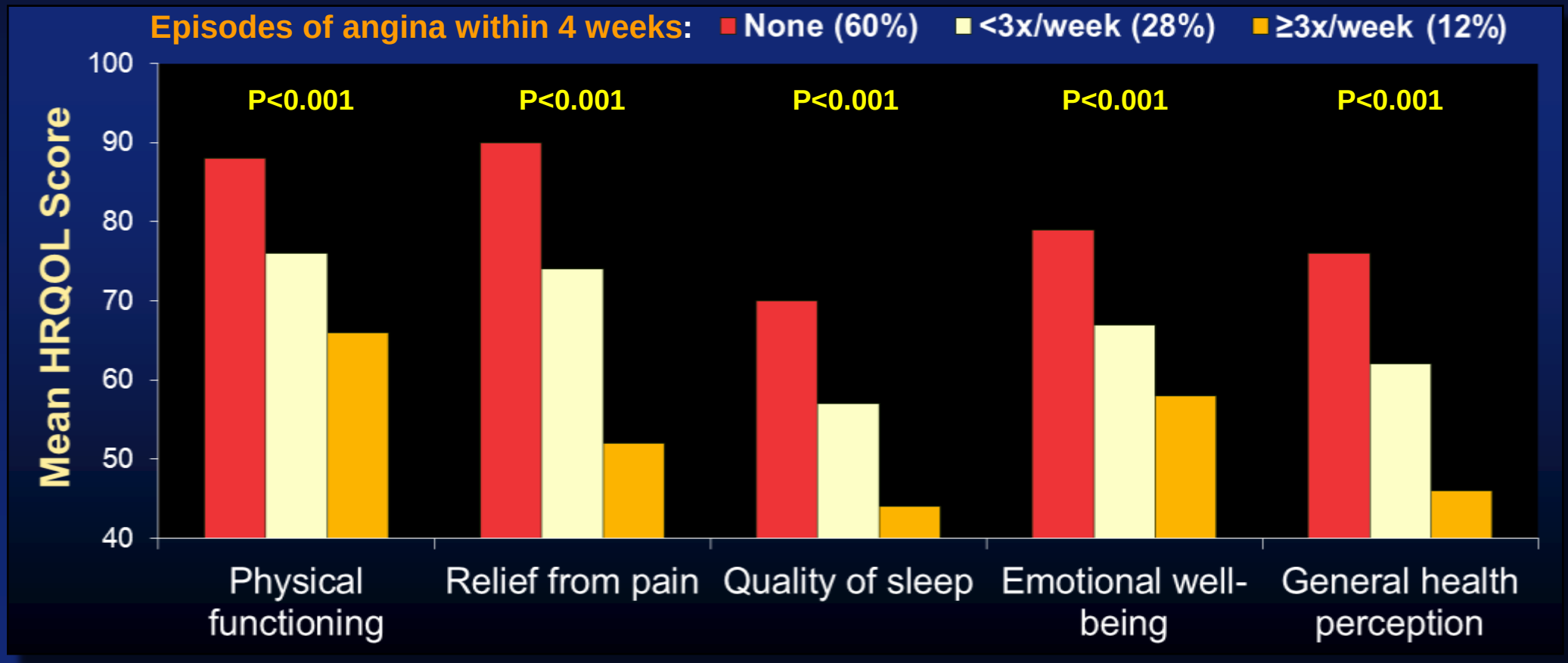
ABSORB Clinical Program Slides; TCT 2014

SGE; 0414-6, 17

MERLIN: Implications of Chronic Stable Angina Before and After Revascularization

827 pts aged 55–79 yrs in Sweden with CSA who underwent PCI or CABG in 1994 or 1995 and completed a baseline and 4-year HRQOL survey

Status 4 years after revascularization



Brorsson B et al. Heart 2002;87:140–5

SPIRIT IV: Consequences of Angina

2,051 non-complex* Xience V PCI pts

- **542 (26.4%) angina within 1 year**
  - **129 (23.8%) with revasc**
  - **413 without revasc**
- **1,509 no angina**
  - **16 (1.1%) with revasc**
  - **1,493 without revasc**

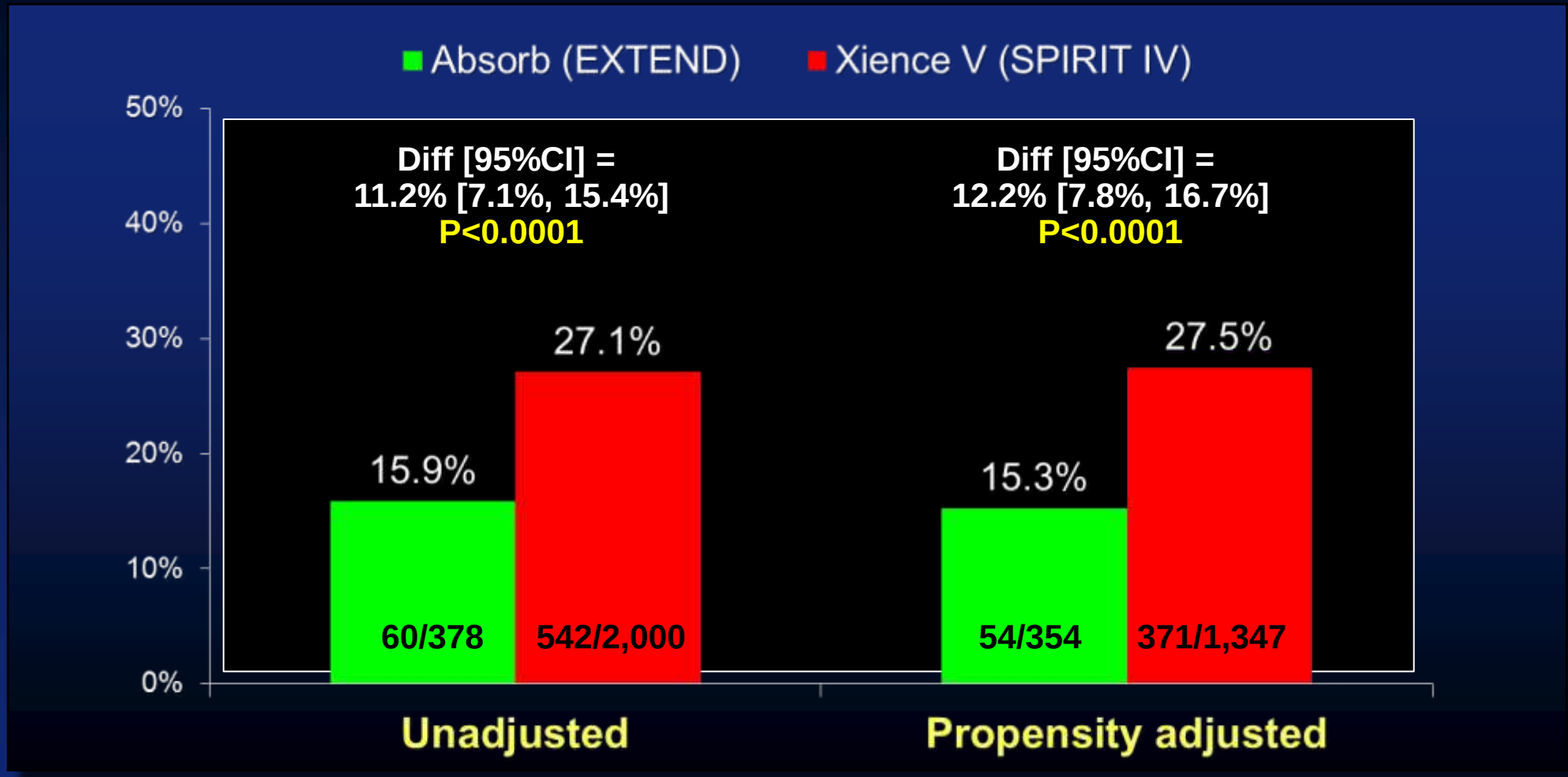
Ischemia-driven	
TLR	8.1%
TVR	13.7%
Non-TVR	11.8%
All	23.6%

Treatment of all pts with angina	
Medication change	39.2%
Hospitalized	35.6%
Diagnostic angiogram	40.9%
PCI	21.6%
CABG	3.1%
Pacer/ICD	1.3%
Any treatment Δ	72.9%

*Excludes complex pts and lesions (3 vessel PCI; PCI of 2 lesions per vessel; RCA aorto-ostial lesions; bifurcation lesions

SGE; 0414-7, 10

Angina Recurrence by 1-Year: EXTEND* vs. SPIRIT IV**



*Excludes non-Japanese Asian pts because of low event reporting rates; **Excludes complex pts and lesions (3 vessel PCI; PCI of 2 lesions per vessel; RCA aorto-ostial lesions; bifurcation lesions)

Data on file, Abbott Vascular

SGE; 0414-6, 20

Post-PCI Angina: Limitations of Current Data

- Much of it is unblinded -> possible placebo and/or ascertainment bias
- Also data were collected prospectively, focus was not on this endpoint

US ABSORB Program and Trial Strategy

Protocol 10-392

ABSORB III
US Approval Trial, n~2250

Lead-in Cohort (n <=50)	Training
Primary Cohort, RCT (n~2000)	Approval SDA claim
Imaging Cohort, RCT RCT (n~200)	Vasomotion, & late lumen growth claims
PK Sub-study (n=12)	Pharmacokinetics

Achieve Approval

ABSORB IV
Continued Access Trial, (n~3000)

- A prospective, randomized (1:1, Absorb BVS to XIENCE), single-blind, multi-center study
- ~3000 subjects at ~132 sites.
- Enrollment to start once the AIII primary cohort completes enrollment

Show superiority of Absorb to XIENCE

ABSORB Clinical Program Slides; TCT 2014

ABSORB IV Randomized Controlled Trial

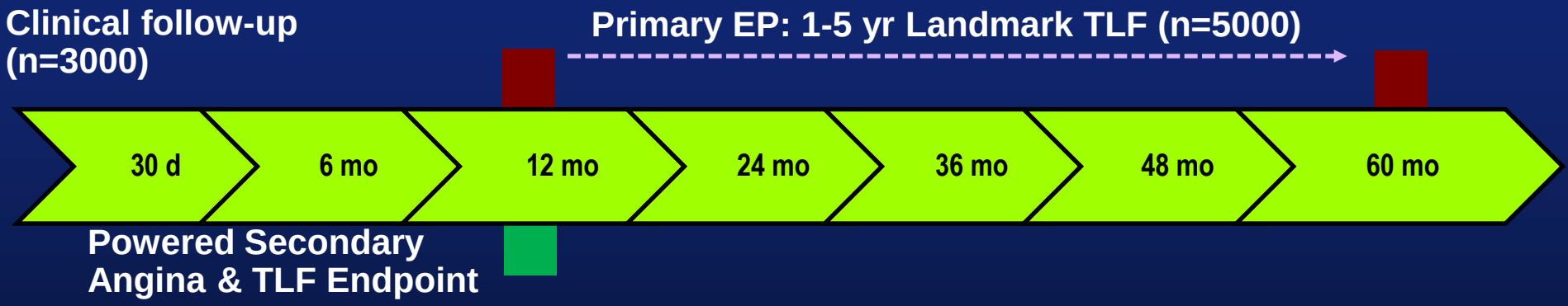
- Principal Investigator: Gregg Stone
- Study Co-PIs: Dean Kereiakes & Stephen Ellis

Evaluate safety and effectiveness of Absorb BVS in up to two *de novo* lesions in separate epicardial vessels

RVD 2.5 mm – 3.75 mm; Lesion length ≤ 24 mm

ABSORB IV Randomized Controlled Trial

Prospective, single blind, randomized 1:1 Absorb BVS vs. XIENCE
Up to 3000 patients in up to 132 US and non-US sites



Primary Endpoint	Target Lesion Failure (TLF), between 1 and 5 years, tested first for non-inferiority of Absorb BVS to XIENCE with reflex testing to superiority Analysis will include 3000 ABSORB III and 2000 ABSORB IV subjects (n=5000)
Powered Secondary Endpoints	1) The percentage of patients who experienced angina within 1 year, tested first for non-inferiority of Absorb BVS to XIENCE with reflex testing to superiority 2) TLF through 1 year, tested for non-inferiority of Absorb BVS to XIENCE.

ABSORB Clinical Program Slides; TCT 2014

ABSORB Japan
Single blind, Randomized (2:1), Active Controlled Trial in Japan

Max 2 *de novo* coronary lesions,
Max 1 lesion per epicardial vessel,
Lesion length ≤ 24 mm; Dmax 2.5mm – 3.75 mm

400 Subjects

38 sites

Stent Diameters
2.5, 3.0, 3.5 mm

Stent Lengths
8* 12, 18, 28 mm
* Bailout

FPI: Apr 27, 2013
LPI: Dec 27, 2013

Absorb BVS
N ~ 267

XIENCE PRIME
N ~ 133

Clinical FUP	30d	6mo	12mo	13mo	24mo	36mo	48mo	60mo

Study Objective:	**To evaluate the safety and effectiveness of the Absorb BVS in treatment of subjects with ischemic heart disease caused by de novo native coronary artery lesions**
Primary Endpoint: Secondary Endpoints:	TLF at 1 year (non-inferiority) 13 months LL (non-inferiority); 3 year NTG induced vasodilatation, by QCA (superiority); Delta average lumen area post-procedure to 3 year, by IVUS (superiority)

ABSORB China
Randomized (1:1), Active Controlled Trial in China

Up to two *de novo* native coronary artery lesions (single target lesion or one target and one non-target lesions, or two target lesions, each in separate epicardial vessels)
Lesion length ≤ 24 mm; RVD 2.5mm – 3.75 mm

~473 Subjects

Approx. 20-25 sites

Scaffold Diameters	Scaffold Lengths
2.5, 3.0, 3.5 mm	12, 18, 28 mm

BVS (N ~ 237)

XIENCE V (N ~ 236)

Clinical follow-up

*** Angio F/U**

Study Objective:	To evaluate the safety and effectiveness of the BVS in treatment of subjects with ischemic heart disease caused by de novo native coronary artery lesions
Primary Endpoint:	In-segment late loss at 12 months; non-inferiority to XIENCE V
Secondary Endpoints:	Various angiographic endpoints & clinical endpoints

Thank You