Can We Prevent Future Events of Deferred Lesions ? *PREVENT Trial ;* Design and Rationale

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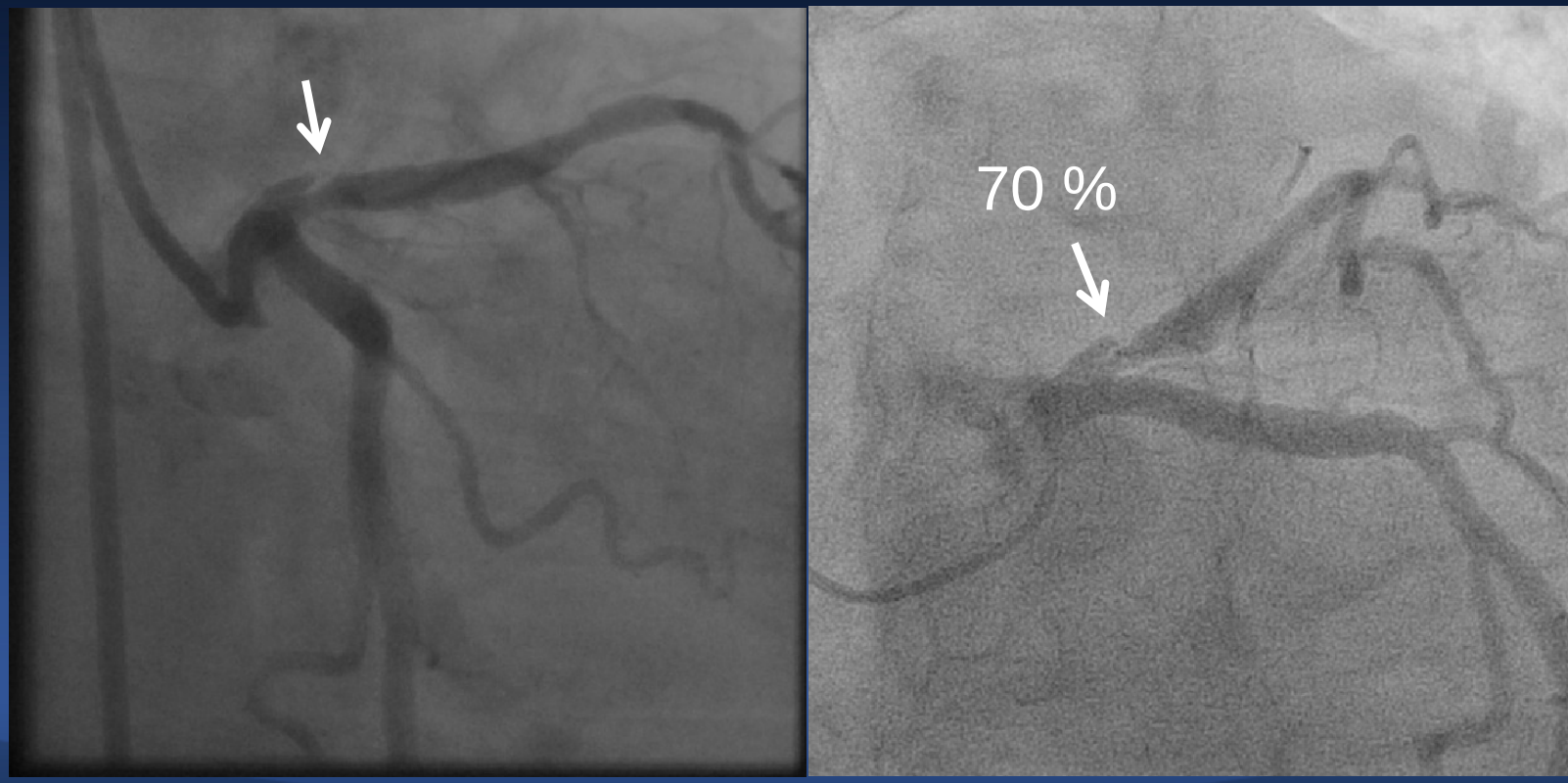
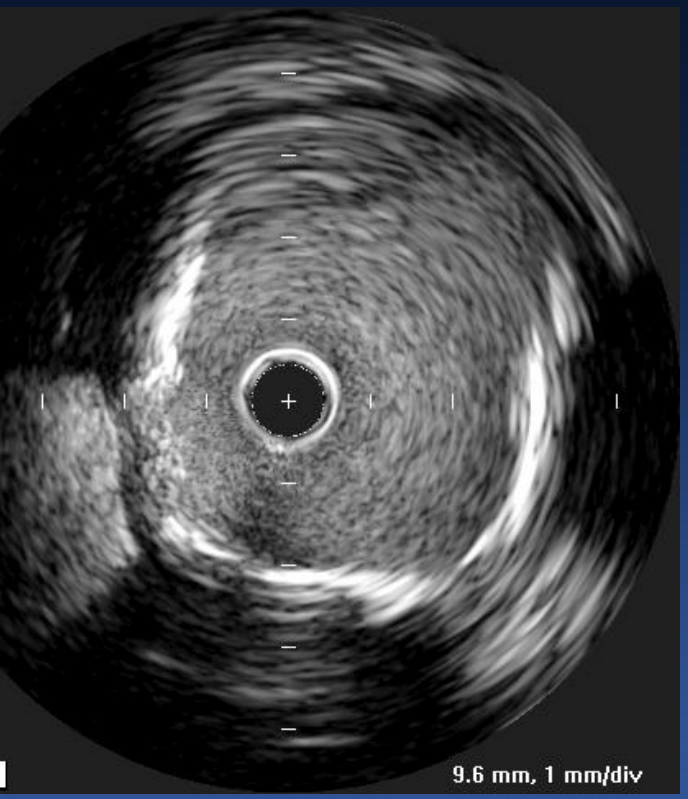
M/74,
Asymptomatic Plaque Rupture

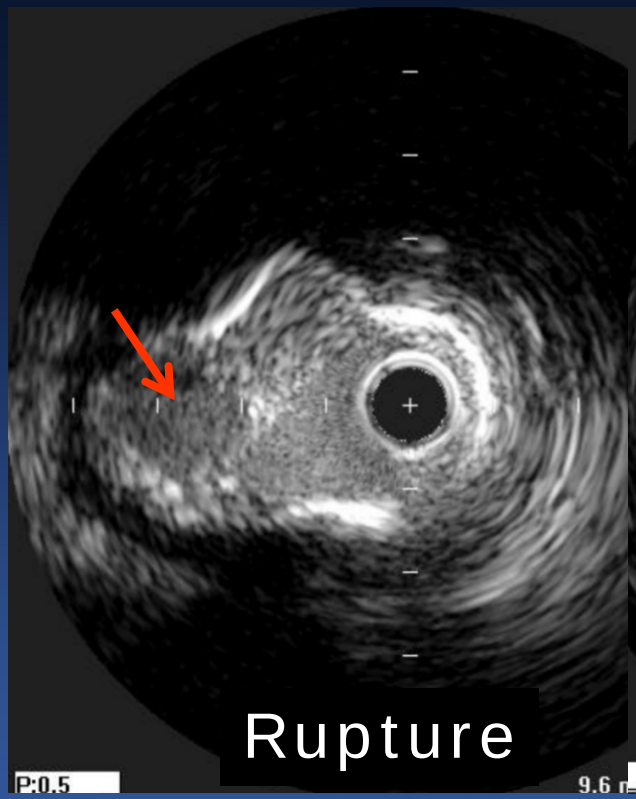
Proximal LAD Stenosis on Coronary CT,
Hypertension, DM, Hyperlipidemia, Ex-smoker

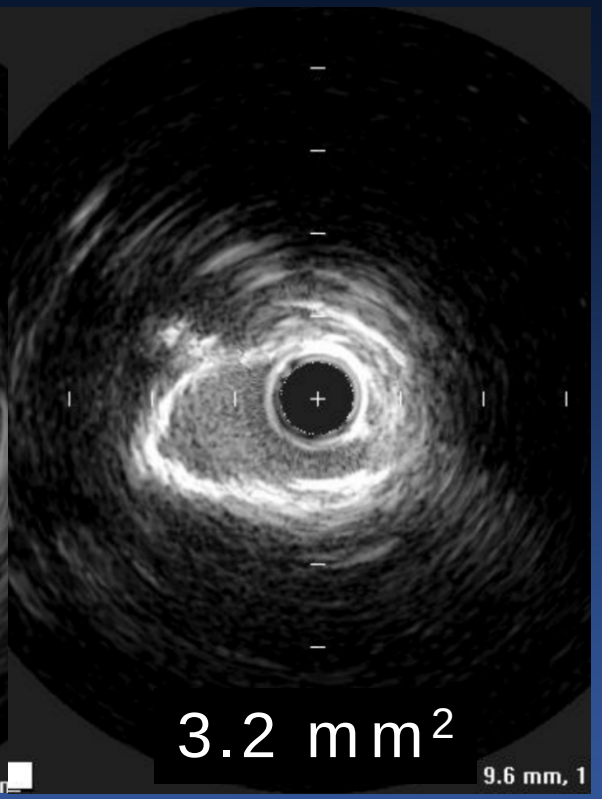


IVUS

LM ***LAD, Culprit***

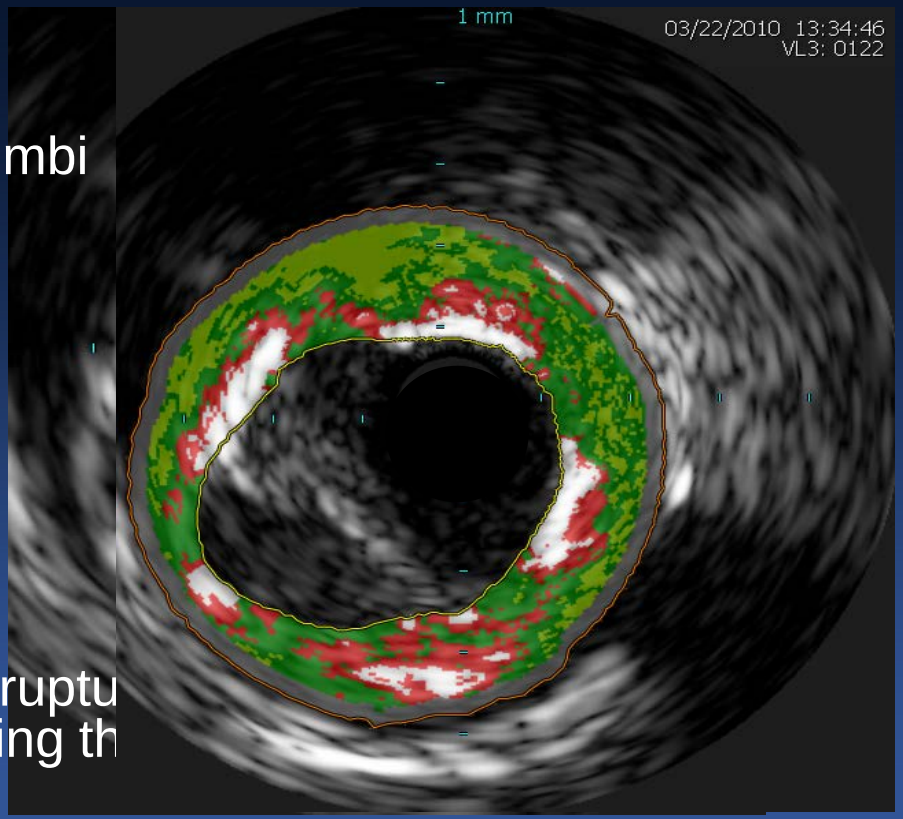






VH-IVUS

LAD, Culprit



Thrombi

Plaque ruptu
organizing th

PB: 71.3%
FI : 41.4%
FF: 20.0%
NC: 23.0%
DC: 15.6%

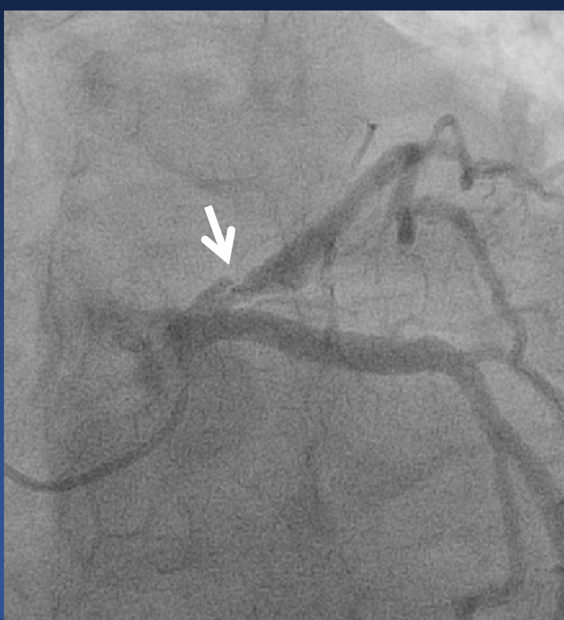
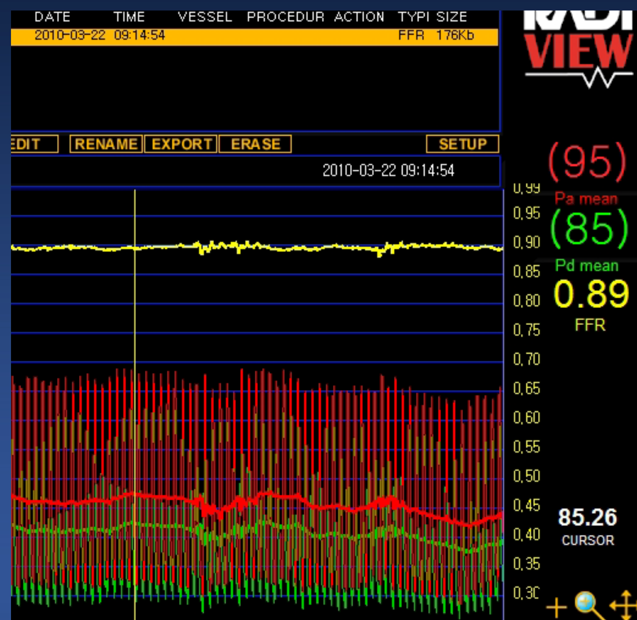
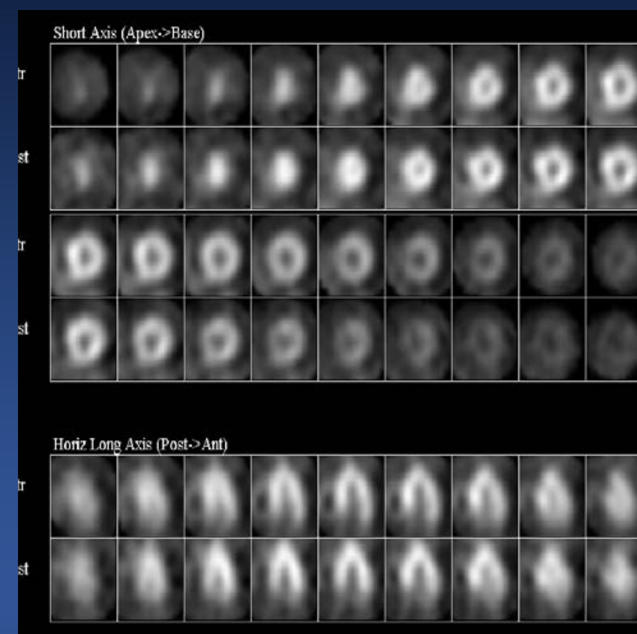
Vulnerable Plaque !

Visual-Functional Mismatches

Vulnerable Plaque with Negative FFR

I Just Defer!

To Treat Based on Plaque Vulnerability, Not To Treat Based on FFR >0.80

Vulnerable Plaque	Negative FFR 0.89	Normal Thallium Spect
		

Why I Defer ?

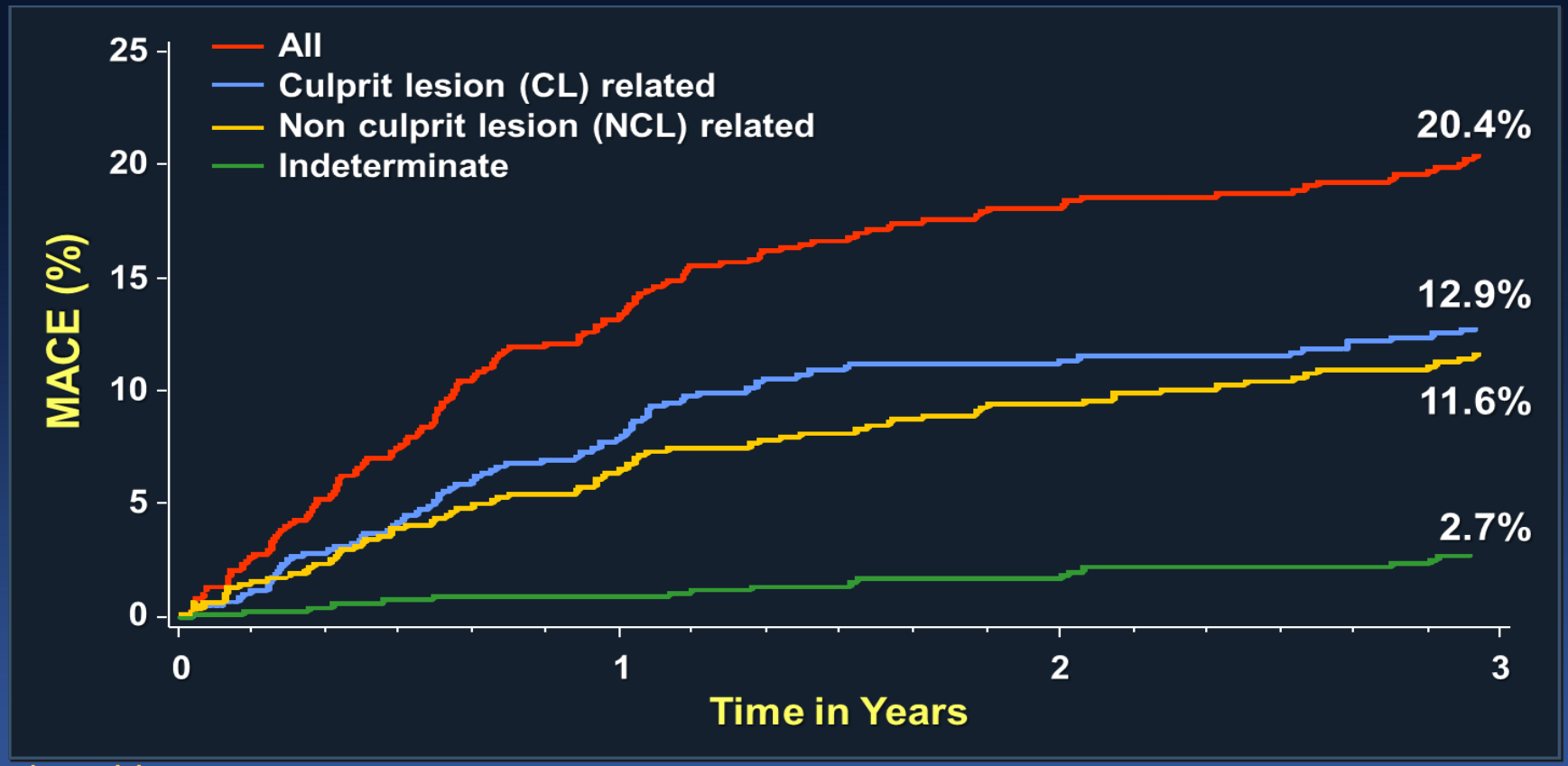
1. I am a FFR believer.
2. FFR is *well matched with non-invasive stress tests.*
3. Negative non-invasive stress tests means *just excellent prognosis (0.6%/year, Cardiac Death and MI),* even in the presence of angiographically proven coronary artery disease.

Shaw LJ, J Nucl Cardiol 2004;11:171-85 ,
Prognostic value of gated myocardial perfusion SPECT.
Very large meta-analysis. (n=39,173 patients)

Q1,
Should We Treat *Functionally Insignificant Vulnerable Plaque* ?

PROSPECT: MACE

(N=700, ACS, 3-Vessel Imaging after PCI)

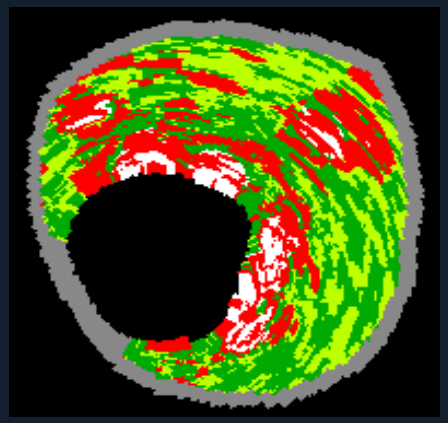


Number at risk				
ALL	697	557	506	480
CL related	697	590	543	518
NCL related	697	595	553	521
Indeterminate	697	634	604	583

Stone GW et al. NEJM 2011;364:226-35

Vulnerable Plaque
Defined by VH-IVUS

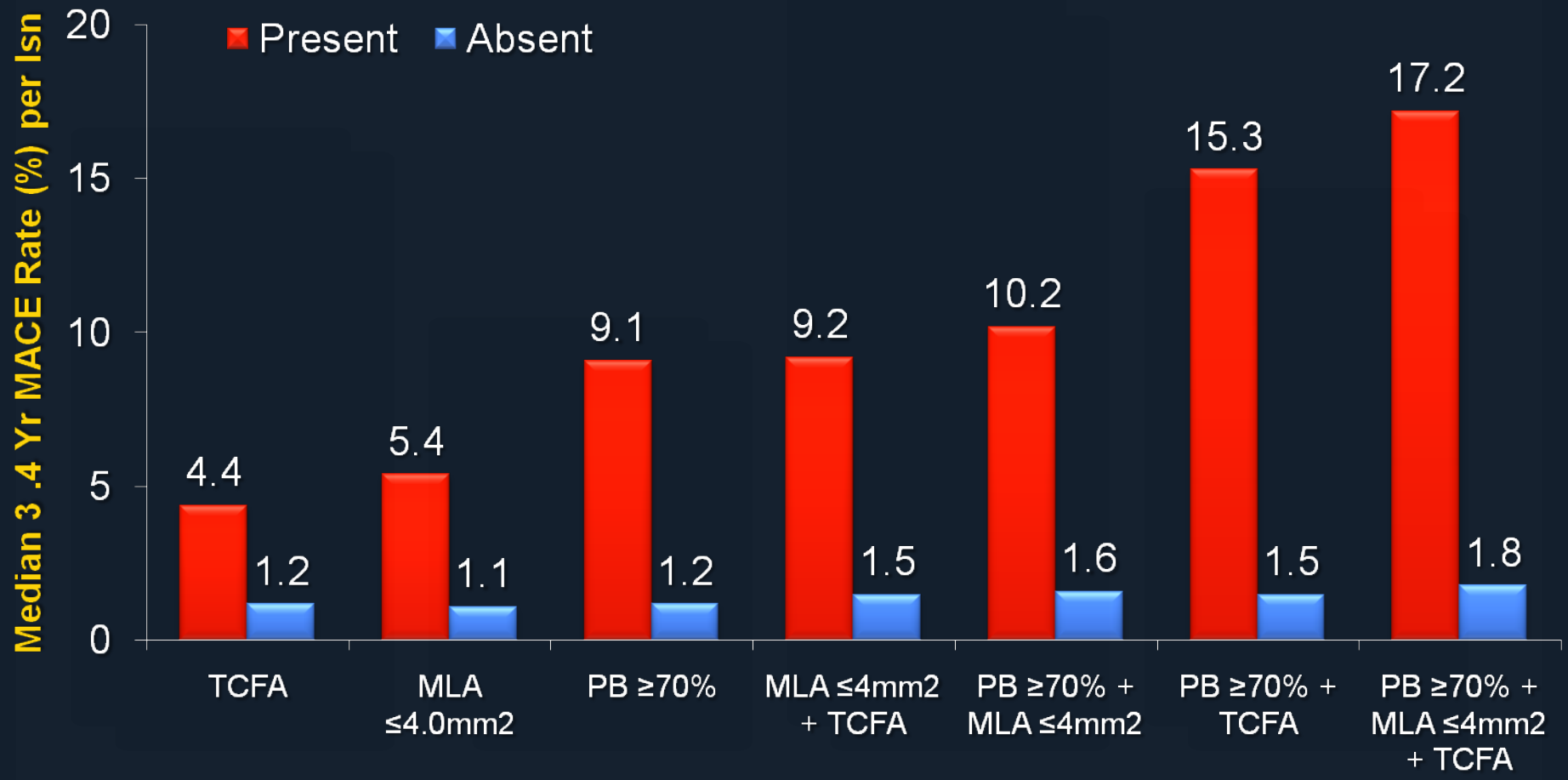
Independent Predictors of Non-Culprit Lesion Events



	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

Stone GW et al. NEJM 2011;364:226-35

PROSPECT: Correlates of Non Culprit Lesion Related Events



	TCFA	MLA ≤4.0mm2	PB ≥70%	MLA ≤4mm2 + TCFA	PB ≥70% + MLA ≤4mm2	PB ≥70% + TCFA	PB ≥70% + MLA ≤4mm2 + TCFA
Prevalence*	51.2%	49.1%	30.7%	17.4%	15.4%	11.0%	4.6%
Lesion HR	3.8 (2.2, 6.6)	5.0 (2.9, 8.7)	7.9 (4.6, 13.8)	6.4 (3.4, 12.2)	6.7 (3.4, 13.0)	10.8 (5.5, 21.0)	10.8 (4.3, 27.2)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001

*Likelihood of one or more such lesions being present per patient. PB = plaque burden at the MLA

PROSPECT II Study

PROSPECT ABSORB

900 pts with ACS after successful PCI

3 vessel IVUS + NIRS (blinded)

≥1 IVUS lesion with ≥70% plaque burden present?

Yes (N=300)

R 1:1

- ABSORB BVS + GDMT (N~150)
- GDMT (N=150)

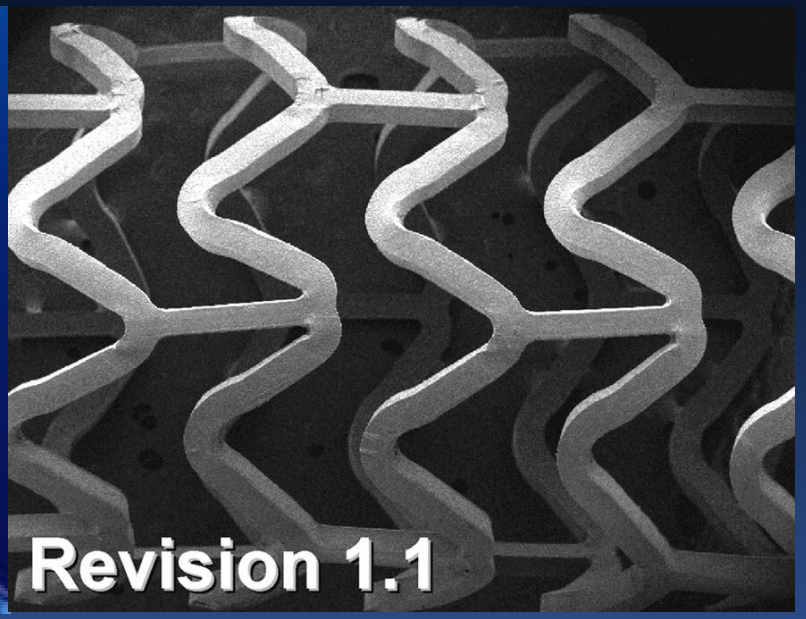
No (n=600)

Routine angio/3V IVUS-NIRS FU at 2 years

Clinical FU for up to 15 years

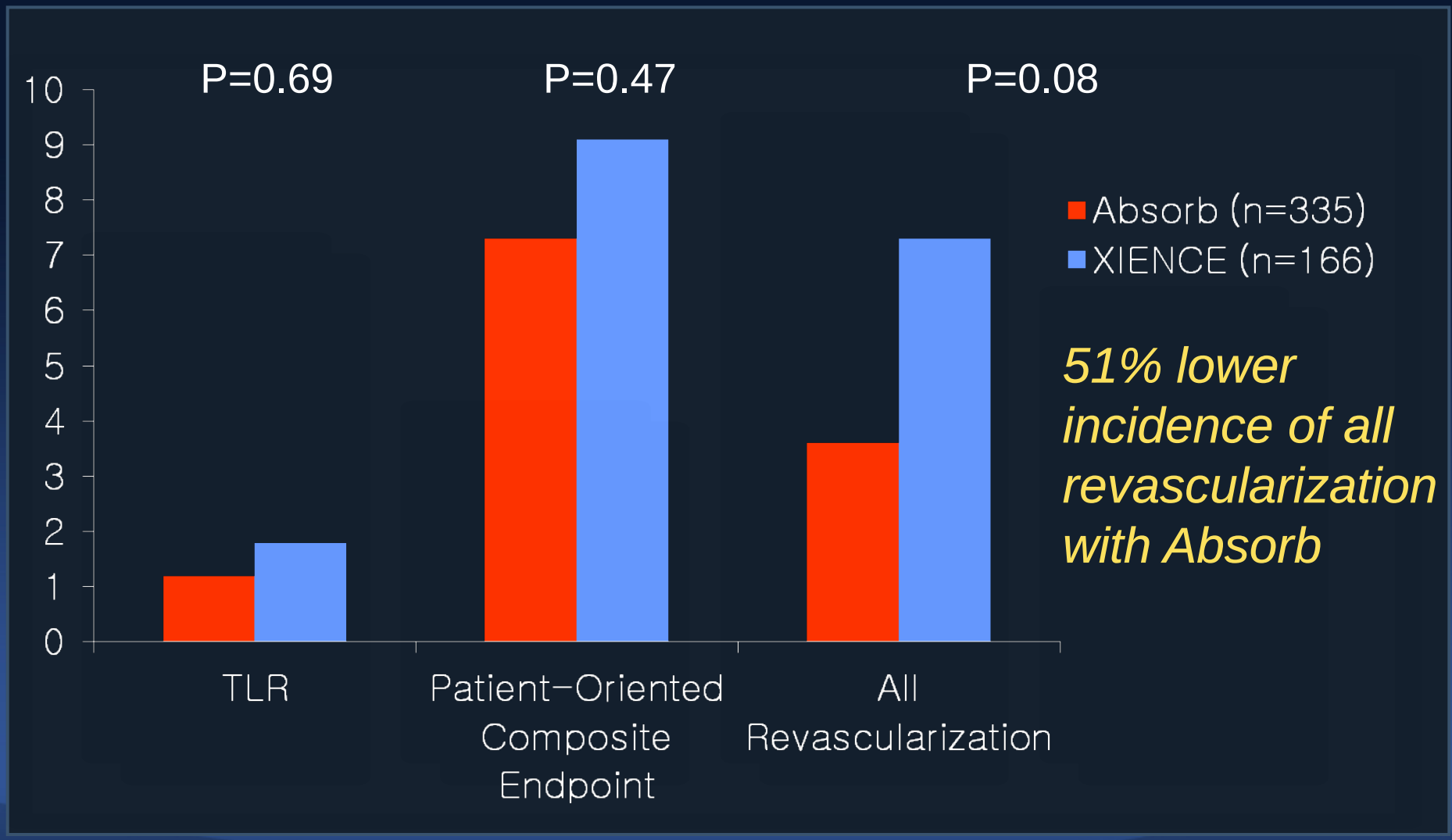
Q2,
Can BVS Implantation Stabilize Plaque Vulnerability ?

Abbott Absorb, Everolimus Eluting BVS



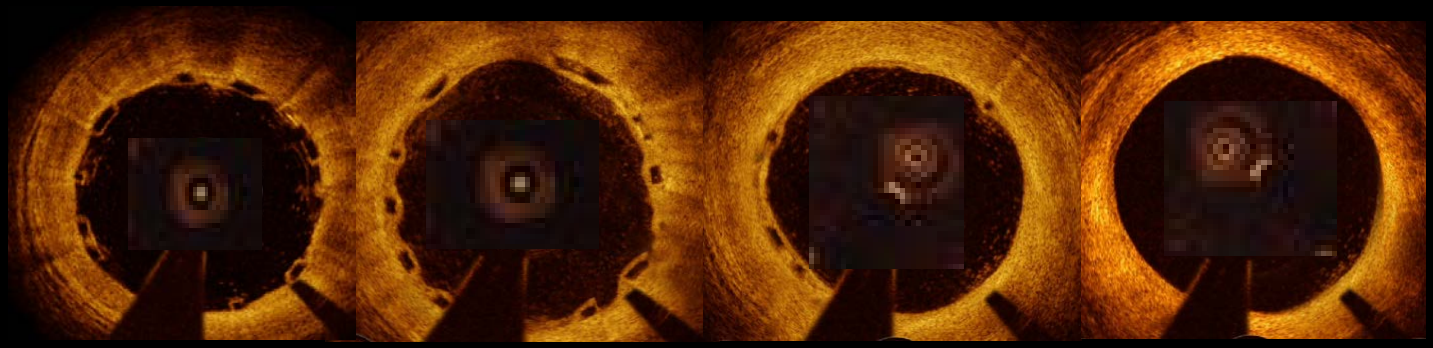
PLLA ; Poly (L-lactide), Multi-link pattern, 150 um

ABSORB II, 1-year Results

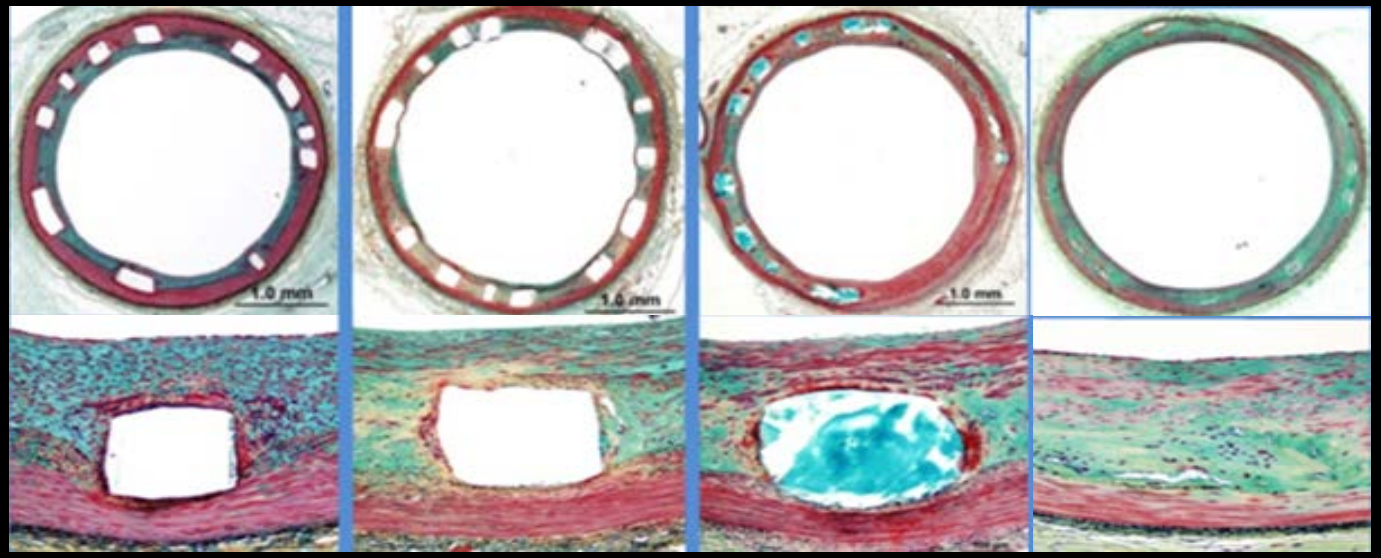


Do their Job and Disappear !

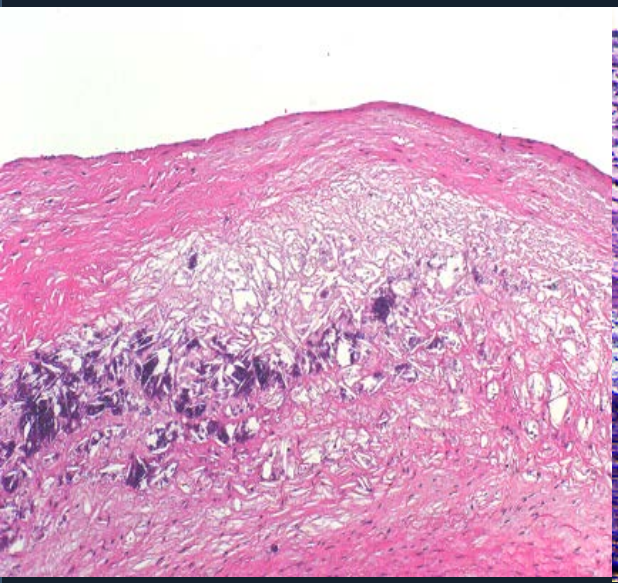
Replaced With SMCs and Myofibroblasts



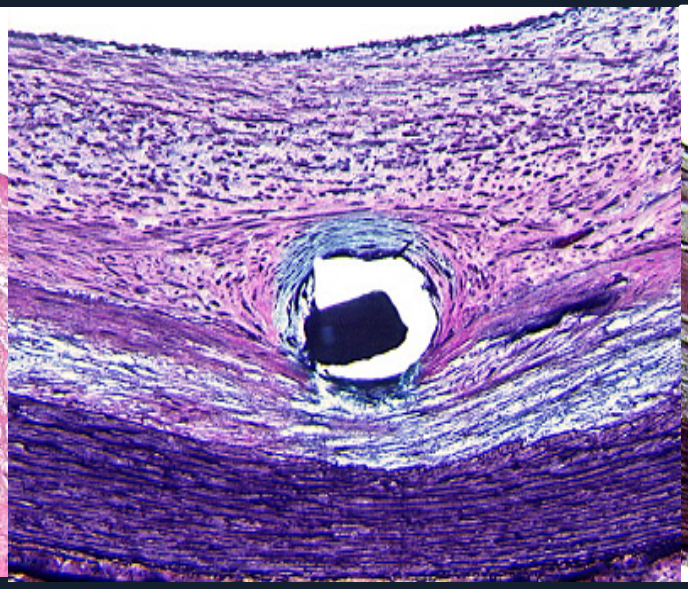
1 month | 6 month | 2 year | 5 year



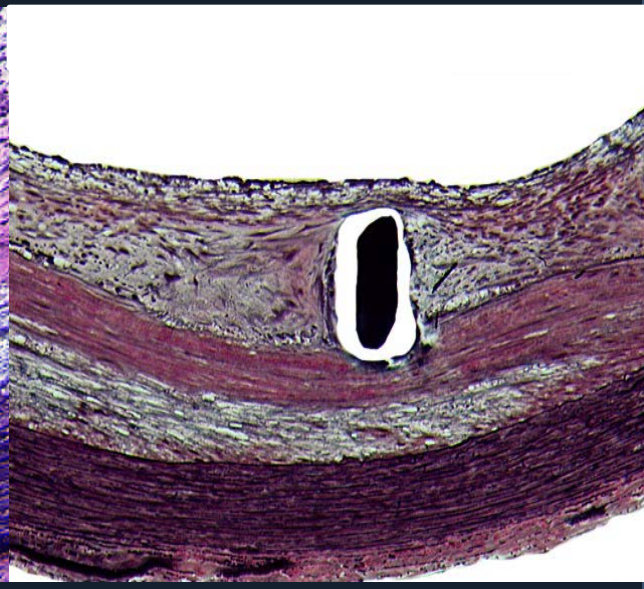
Everolimus Induced Less Neointimal Hyperplasia on TCFA



TCFA



Metallic &
Polymer Strut

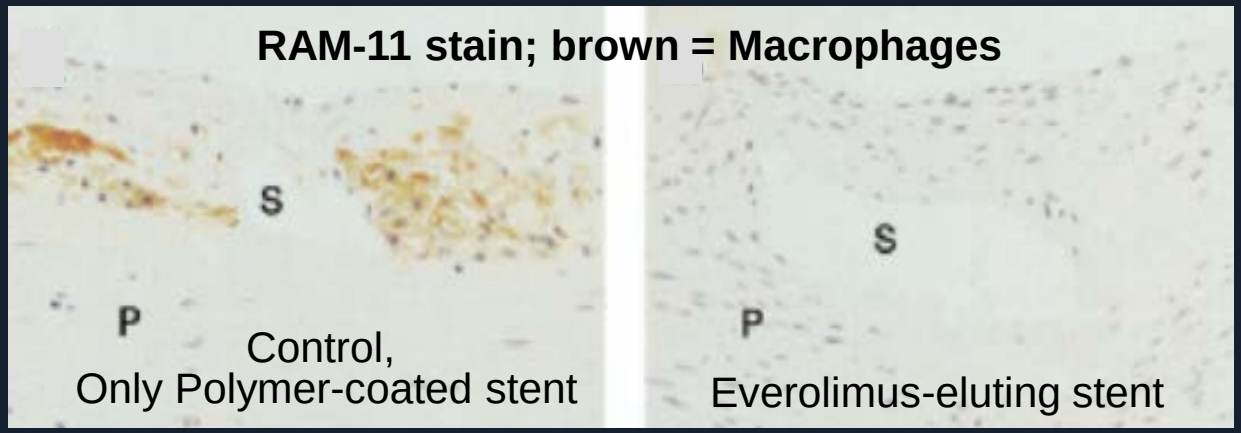


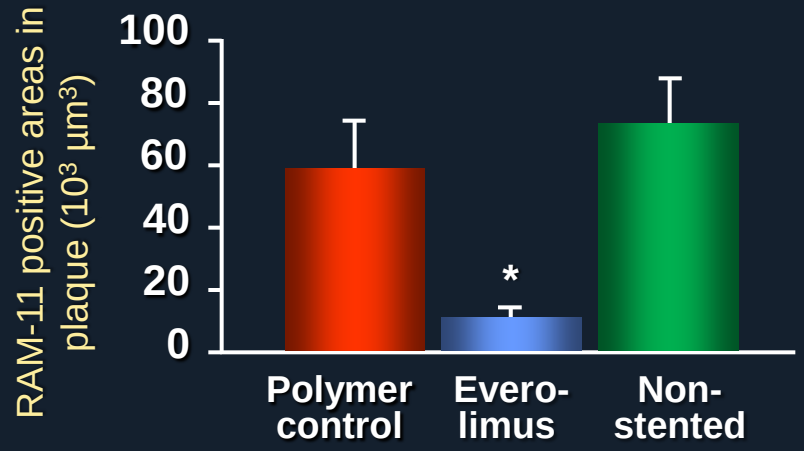
Everolimus Strut

Adapted from Moreno PR.Cardiol Clin 2010;28:1-30

Everolimus Induced, Marked Reduction of Macrophage

Atherosclerotic arteries of cholesterol-fed rabbits

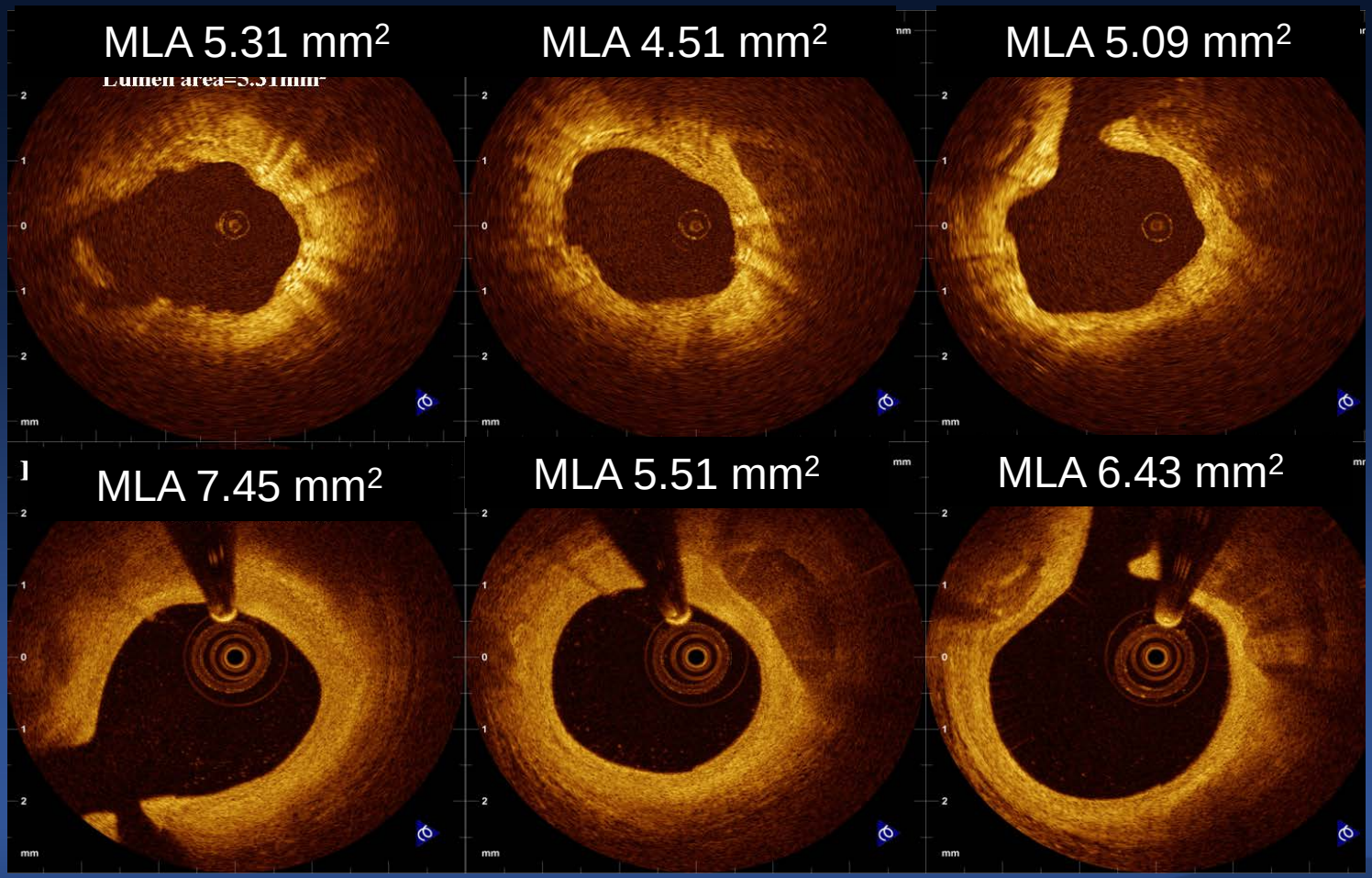




EES resulted in marked reduction of macrophage content, with preservation of SMC, *which can stabilize the plaque vulnerability*

Verheye S et al. JACC 2007;49:706-15

BVS on Vulnerable Plaque, Plaque Stabilization and Lumen Enlargement



Karanasos A et al. Circulation. 2012;126:e89-e91

BVS Implantation

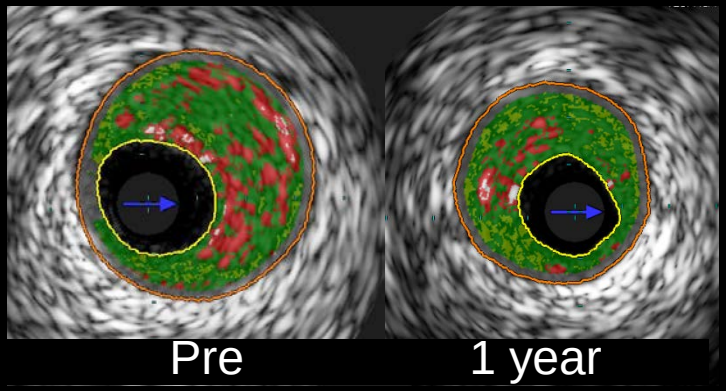
Can Stabilize Plaque Vulnerability And Induce Plaque Regression, Which May Prevent Future Events of Vulnerable Plaque.

Q3,

Can Statin Treatment Stabilize Plaque Vulnerability ?

BVS vs. Statin Treatment

Statin Treatment (Unpublished AMC Data)



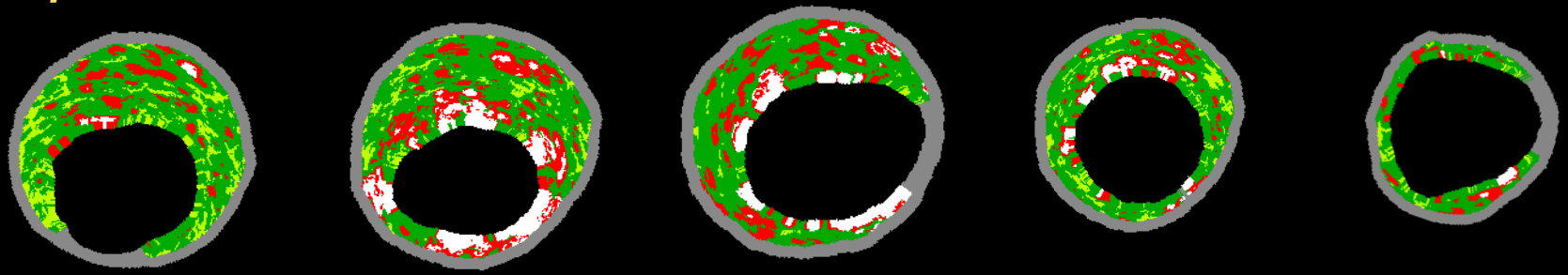
Pre 1 year

	Pre	1 year
Vessel Area	13	12 (8%) ↓
MLA	3.9	3.6 (8%) ↓
Plaque Area	8.6	8.2 (5%) ↓

?

5 years

BVS Implantation



Pre-PCI Post-PCI 6 months 2 years 5 years

Vessel area (mm^2)	15.72	15.34 (3%) ↓	14.09 (10%) ↓	13.76 (12%) ↓
MLA (mm^2)	6.95	6.17 (11%) ↓	6.56 (5.6%) ↓	8.09 (16%) ↑
Plaque area (mm^2)	8.78	9.17 (4%) ↑	7.54 (14%) ↓↓	7.07 (19%) ↓↓

Q4

Can We Prevent Future Events of Vulnerable Plaque ?

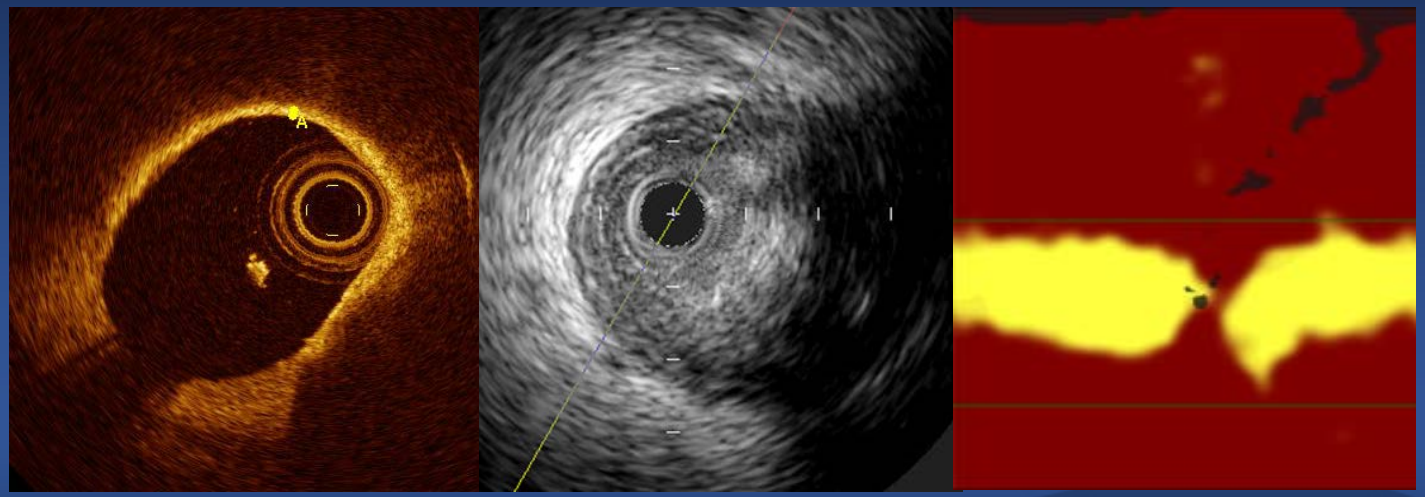
Active Local Treatment Using BVS vs.
Optimal Medical Treatment with Statin

PREVENT Study,

The ***PREVENT***ive Implantation of BVS on Stenosis With Functionally Insignificant Vulnerable Plaque.

Functionally Insignificant (FFR >0.80), ***Vulnerable Plaque***

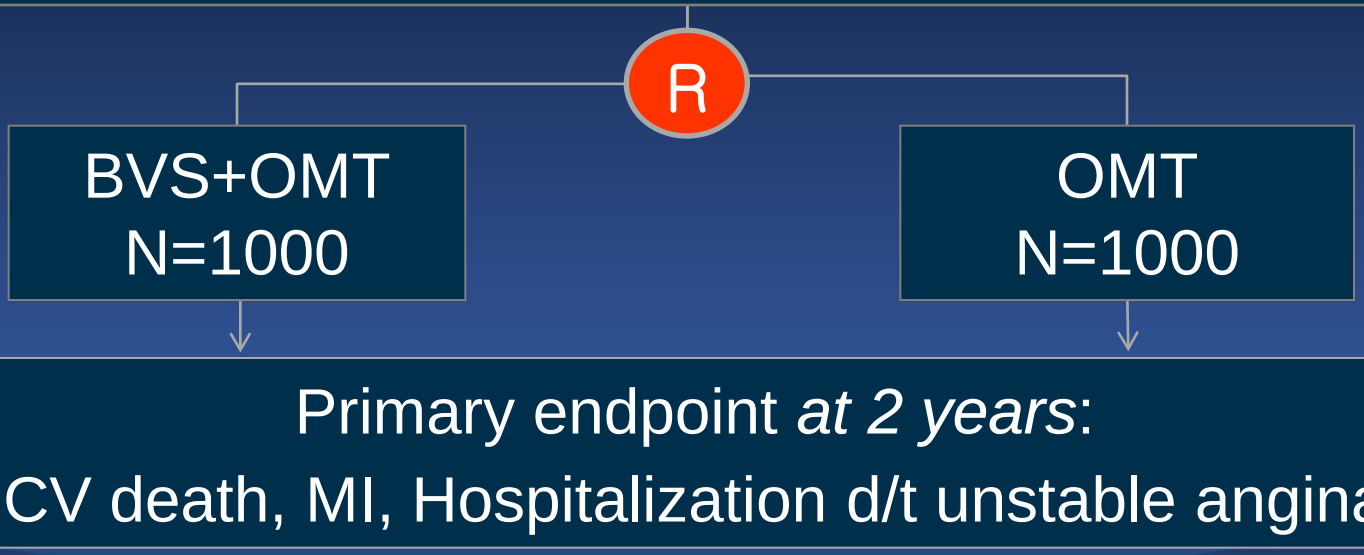
1. TCFA by OCT (<65 um and >90 degree arc)
2. PB_{MLA} ≥70%
3. MLA ≤4.0 mm^2
4. LRP on NIRS ($_{max}LCBI_{4mm}$>500)



PREVENT Trial

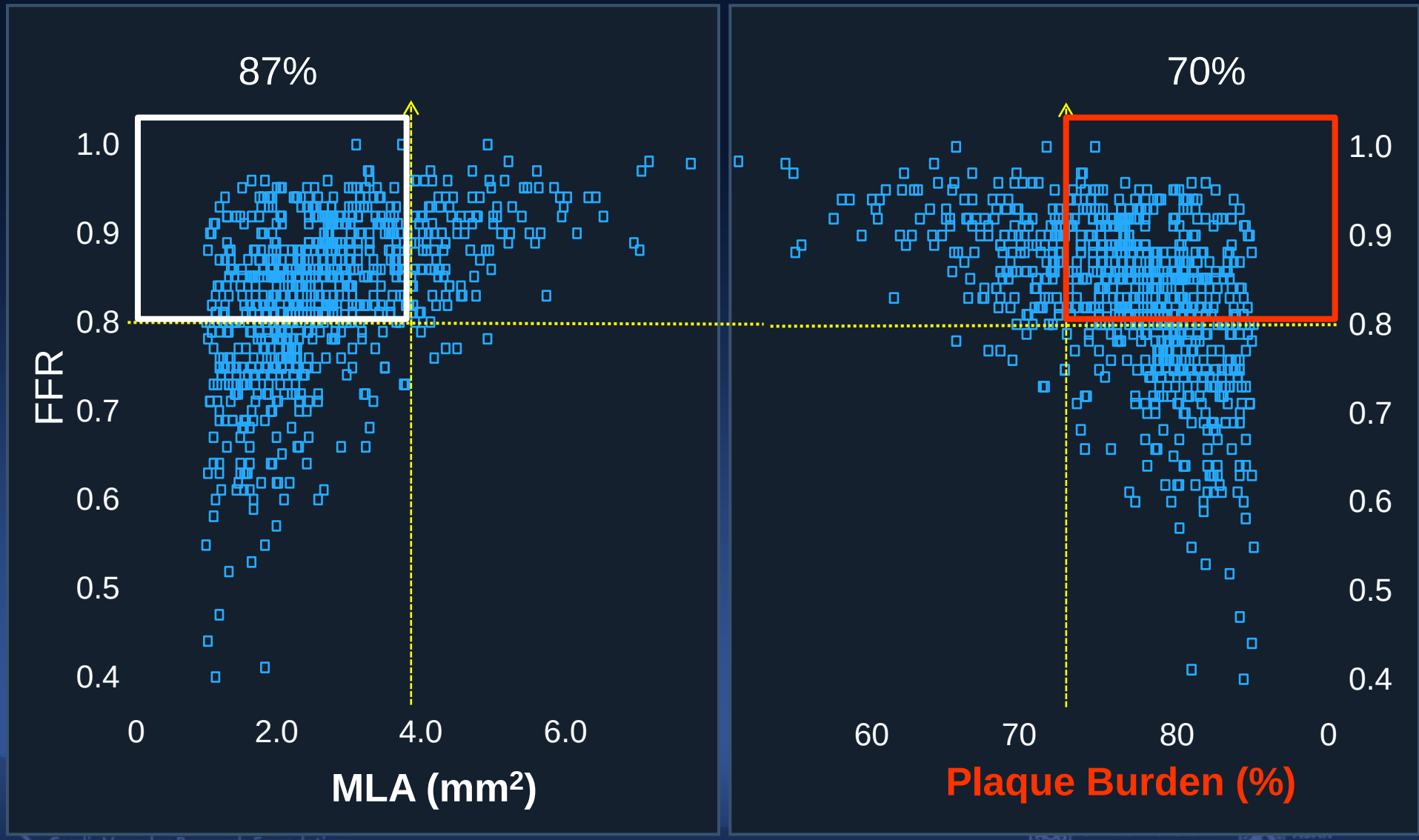
Any Epicardial Coronary Stenosis **with**
FFR ≥0.80 **and with** ***Two*** **of the following**

1. TCFA by OCT (<65 um and >90 degree arc)
2. IVUS MLA ≤4.0mm^2
3. IVUS Plaque Burden >70%
4. Lipid-Rich Plaque on NIRS ($_{max}LCBI_{4mm}$>500)



OCT sub-study/ NIRS sub-study, (300 patients in each arm at 2 years)

Patients Candidate



Objective,

To determine whether BVS implantation on functionally insignificant vulnerable plaque, reduce the incidence of the composite of MACEs compared with optimal medical therapy alone.

A prospective, randomized, multicenter, clinical trial with ‘all comers’ design. Approximately 2,000 patients will be enrolled from international heart centers.

Inclusion Criteria

Age 18 years or older,
Symptomatic or asymptomatic coronary stenosis,
    Eligible for PCI, with
FFR >0.80 and met the two of the following

1. TCFA by OCT (<65 um and >90 degree arc)
2. IVUS MLA<4mm2
3. IVUS plaque burden>70%
4. Lipid-rich plaque on NIRS ($_{max}LCBI_{4mm}$>500)

Exclusion Criteria

Contraindication to dual antiplatelet therapy, Life expectancy <2y, Planned cardiac surgery or planned major non cardiac surgery, Preferred treatment for CABG, STEMI, Bypass graft lesion, Woman who are breastfeeding, pregnant or planning to become pregnant during the course of the study.

Primary and Major Secondary End Point,

The primary endpoint is the 2-year MACE (cardiovascular death, nonfatal MI, unplanned rehospitalization due to unstable angina).

The secondary endpoints include overall MACE, non-urgent revascularization, and rate of cerebrovascular event.

PREVENT Trial

Principal Investigators
Seung-Jung Park, MD, PhD.
Korea

Co-Principal Investigator
Gregg Stone, MD, PhD.
USA

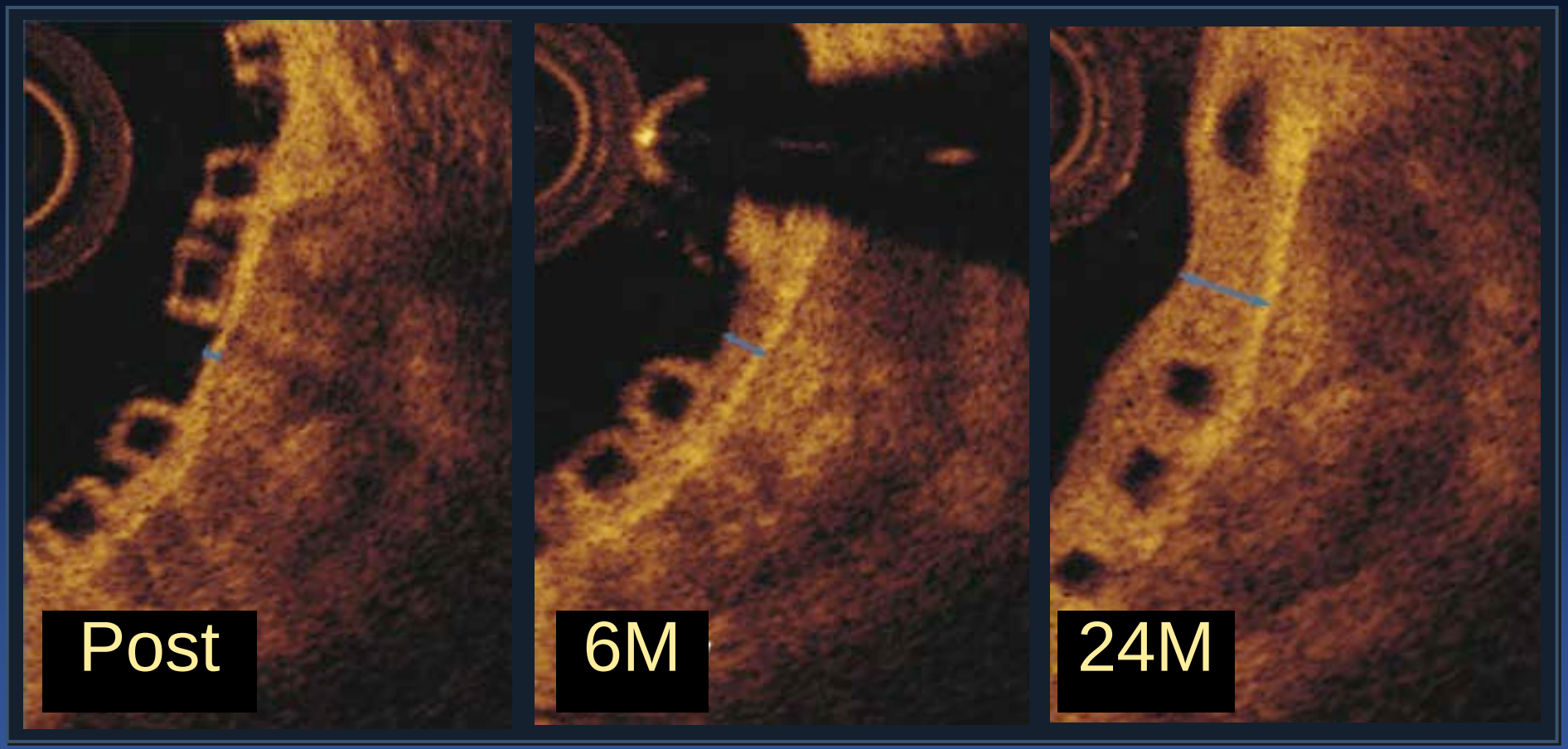
Active Participants
Major 10 centers more in Korea
Dr. Takashi Akasaka, Japan
3-4 centers more in Japan
Dr. Kao in Taiwan China

Ron Waksman, MD. USA
Alan Young, MD.USA
David Cohen, MD. USA
Antonio Colombo, MD. Italy

Thank You !!

summitMD.com

BVS Over A Calcified Plaque, Sealing and Shielding of Plaques



Brugaletta S et al. Atherosclerosis 2012