PREVENT Trial

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Functionally Insignificant (FFR > 0.80) Lesions,

Is Defer (FFR > 0.80) Safe ?

Negative FFR (>0.80 or 0.75)

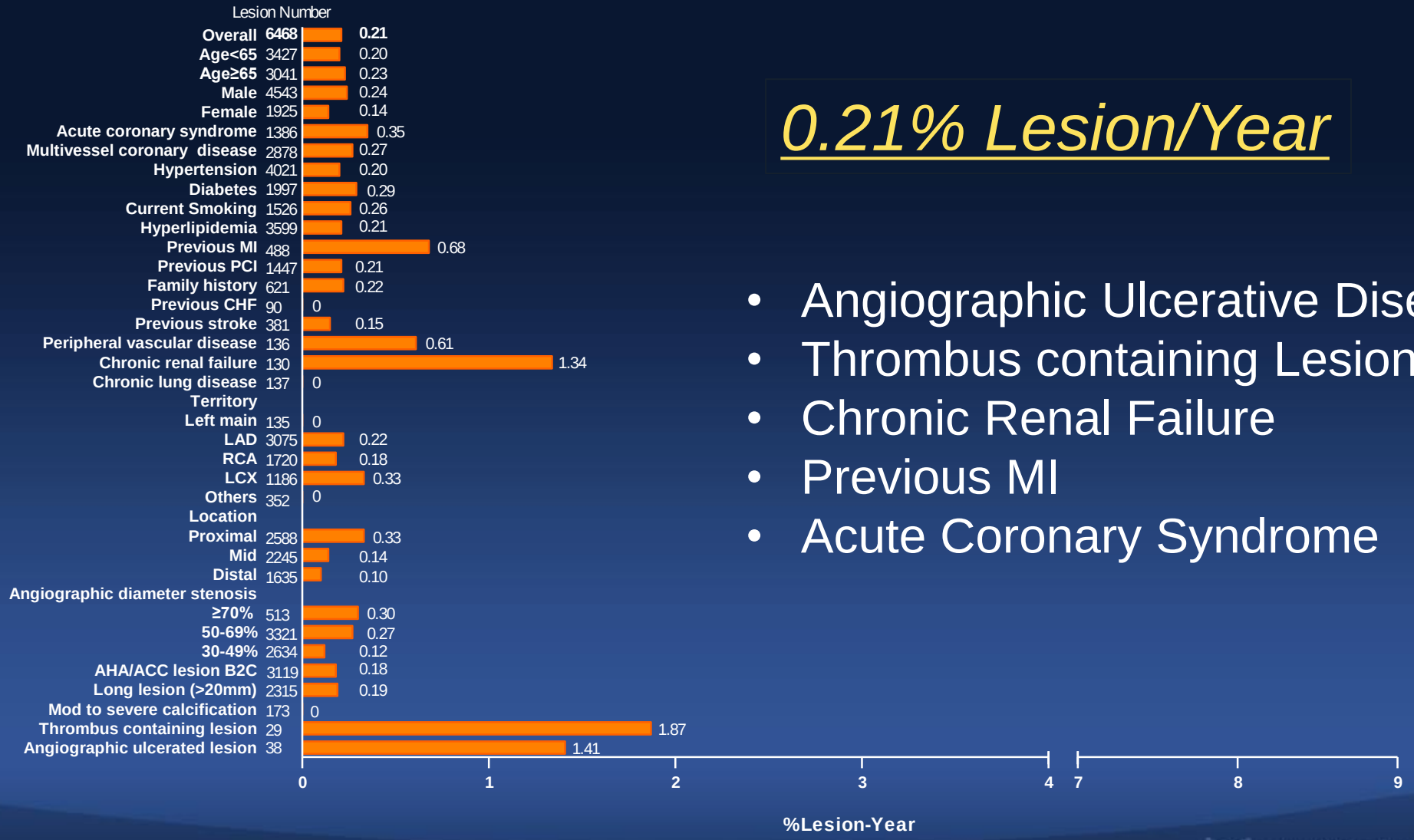
Death and MI / yr

Negative FFR (>0.80 or 0.75) or Negative Non-Invasive Stress Tests: (NUCLEAR studies, DEFER, FAME)	**< 1 %**
Stented Segment : (DEFER, FAME, SYNTAX, and registries)	**2-3 %**
Untreated Positive FFR (<0.75 or 0.80) or Positive Non-invasive Stress Tests: (Registries, ACIP, etc)	**5-10 %**

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

Cardiac Death/MI

(IRIS-FFR Registry, 8633 Deferred Lesions (> 0.80) Analysis, AMC data)



0.21% Lesion/Year

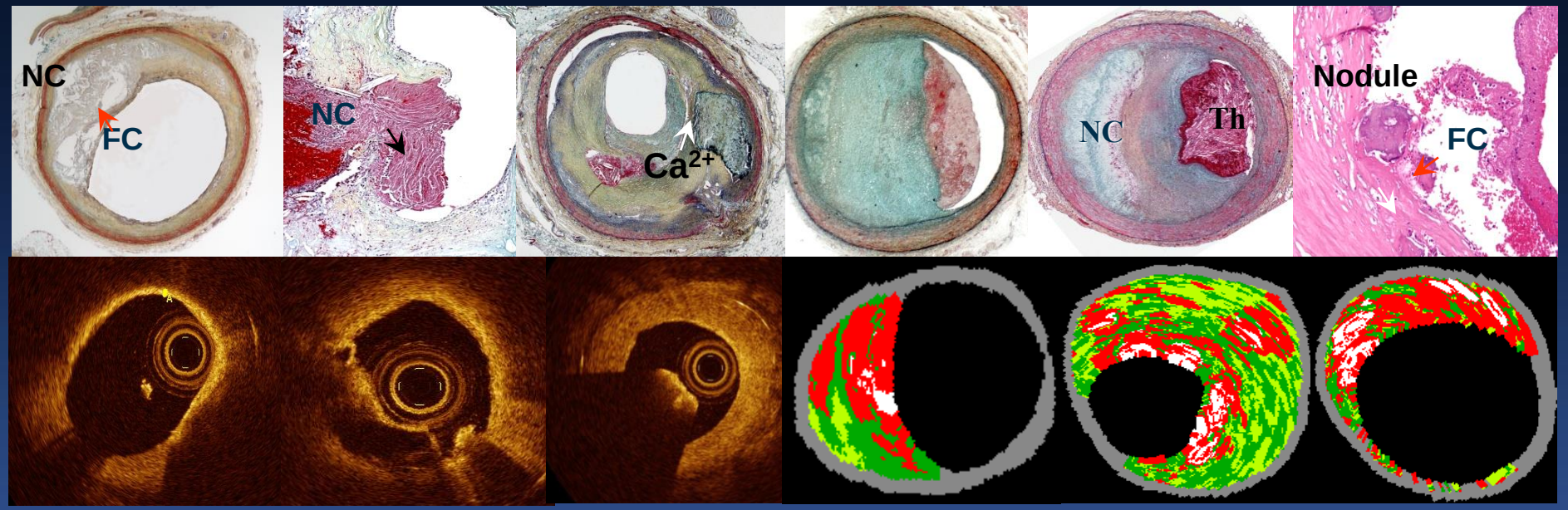
- Angiographic Ulcerative Disease
- Thrombus containing Lesion
- Chronic Renal Failure
- Previous MI
- Acute Coronary Syndrome

Defer (FFR > 0.80) Is Safe and Good !

Negative FFR (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)

Vulnerable Plaque Definition



Virmani R, et al. ATVB 2000;20:1262
Naghavi et al. Circulation 2003;108:1664-72

What is the Vulnerable Plaque?

Vulnerable plaque, also known as "high-risk" or "unstable" plaque, which has a higher likelihood of rupturing and causing a thrombotic event, such as a heart attack or stroke.

Advanced imaging techniques, such as intravascular ultrasound (IVUS) and optical coherence tomography (OCT), are also being used to better visualize and assess plaque vulnerability.

What is the Vulnerable Plaque?

Thin fibrous cap: Vulnerable plaques have a thin outer layer (fibrous cap) covering a lipid-rich core. This thin cap is more prone to rupture, releasing the plaque's contents into the bloodstream and potentially causing a blood clot.

Large lipid core: The lipid-rich core of vulnerable plaques is typically large and composed of cholesterol and other fatty substances. When a plaque ruptures, the lipid core can cause a blood clot, obstructing blood flow and leading to a heart attack or stroke.

What is the Vulnerable Plaque?

Inflammation: The presence of inflammatory cells, such as macrophages and T-cells, within the plaque can contribute to the instability and weakening of the fibrous cap, increasing the likelihood of rupture.

Neovascularization: Vulnerable plaques often have increased blood vessel formation (neovascularization) within them, which can lead to intraplaque hemorrhage and further contribute to plaque instability.

Functionally Insignificant (FFR > 0.80),

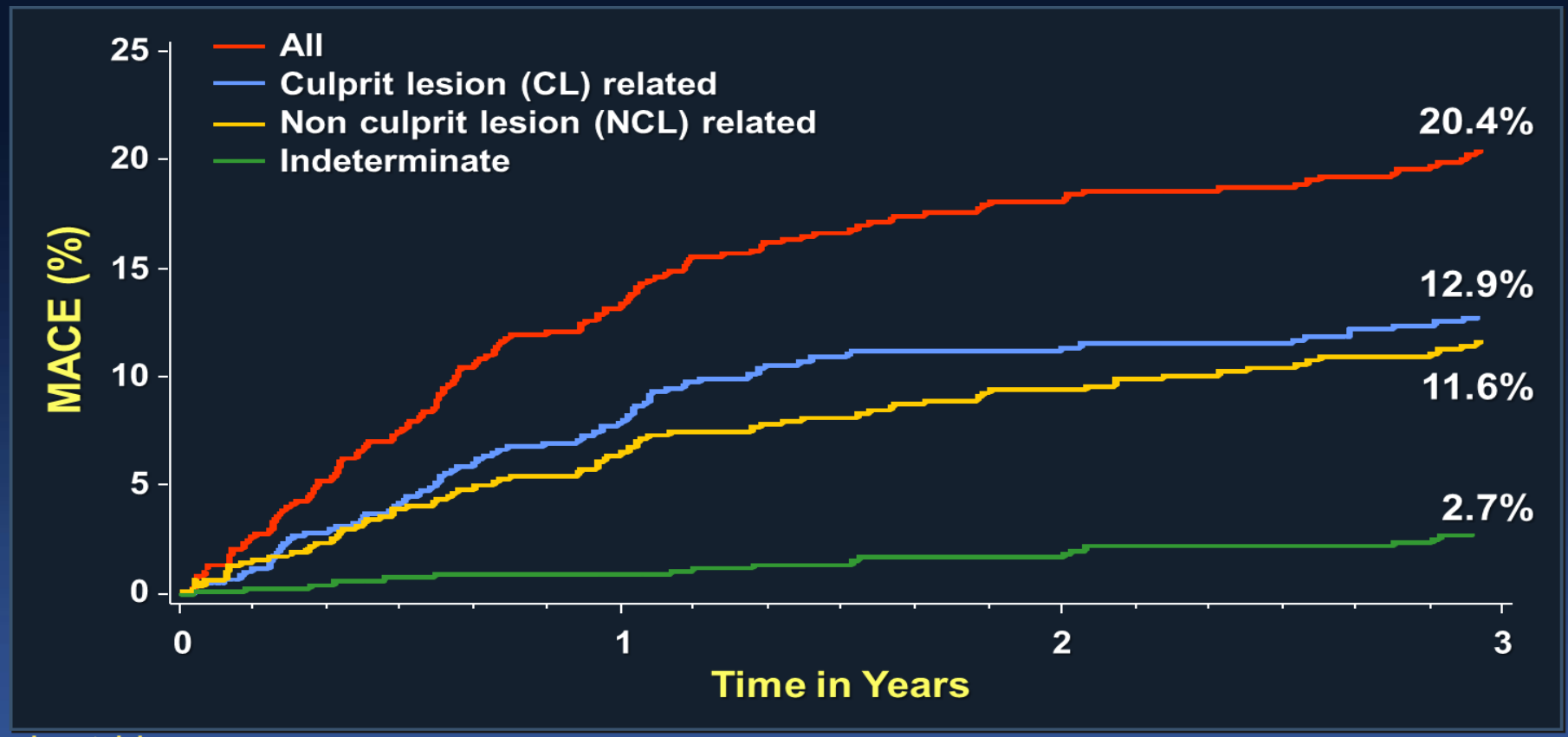
Vulnerable Plaque,

To Treat or Not To Treat ?

Imaging Defined Vulnerable Plaque

PROSPECT: MACE

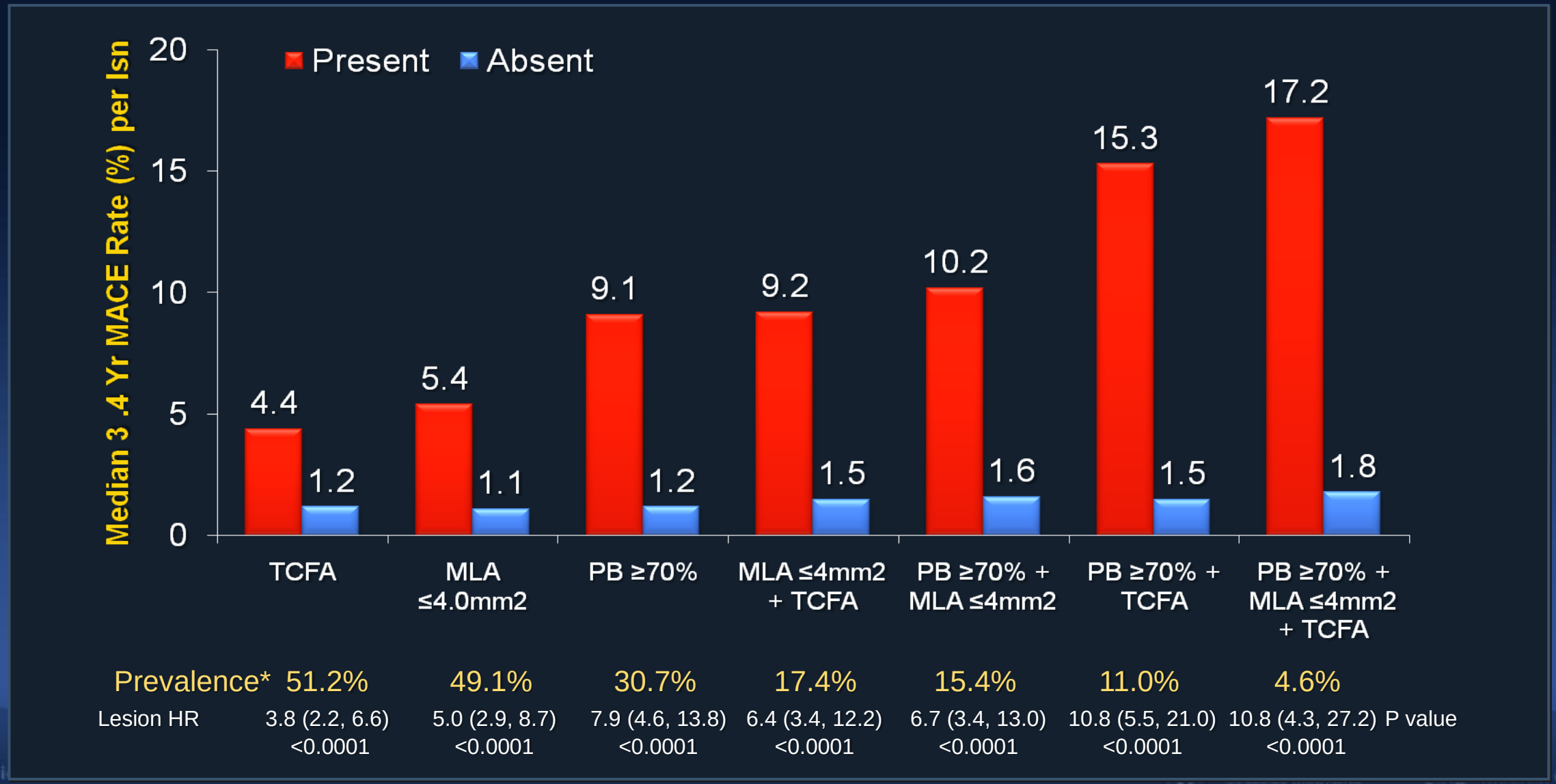
(*N=700, ACS,* 3-Vessel Imaging after PCI)



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

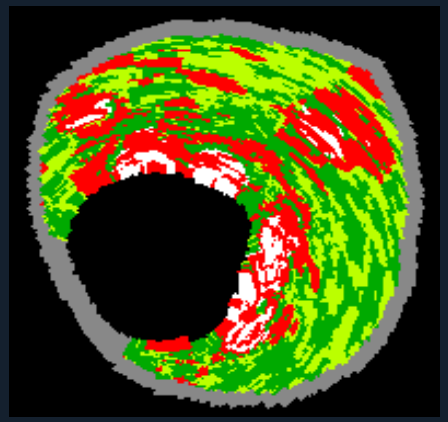
PROSPECT: Correlates of Non Culprit Lesion Related Events



Vulnerable Plaque Defined by VH-IVUS

PROSPECT study

Independent Predictors of Non-Culprit Lesion Events



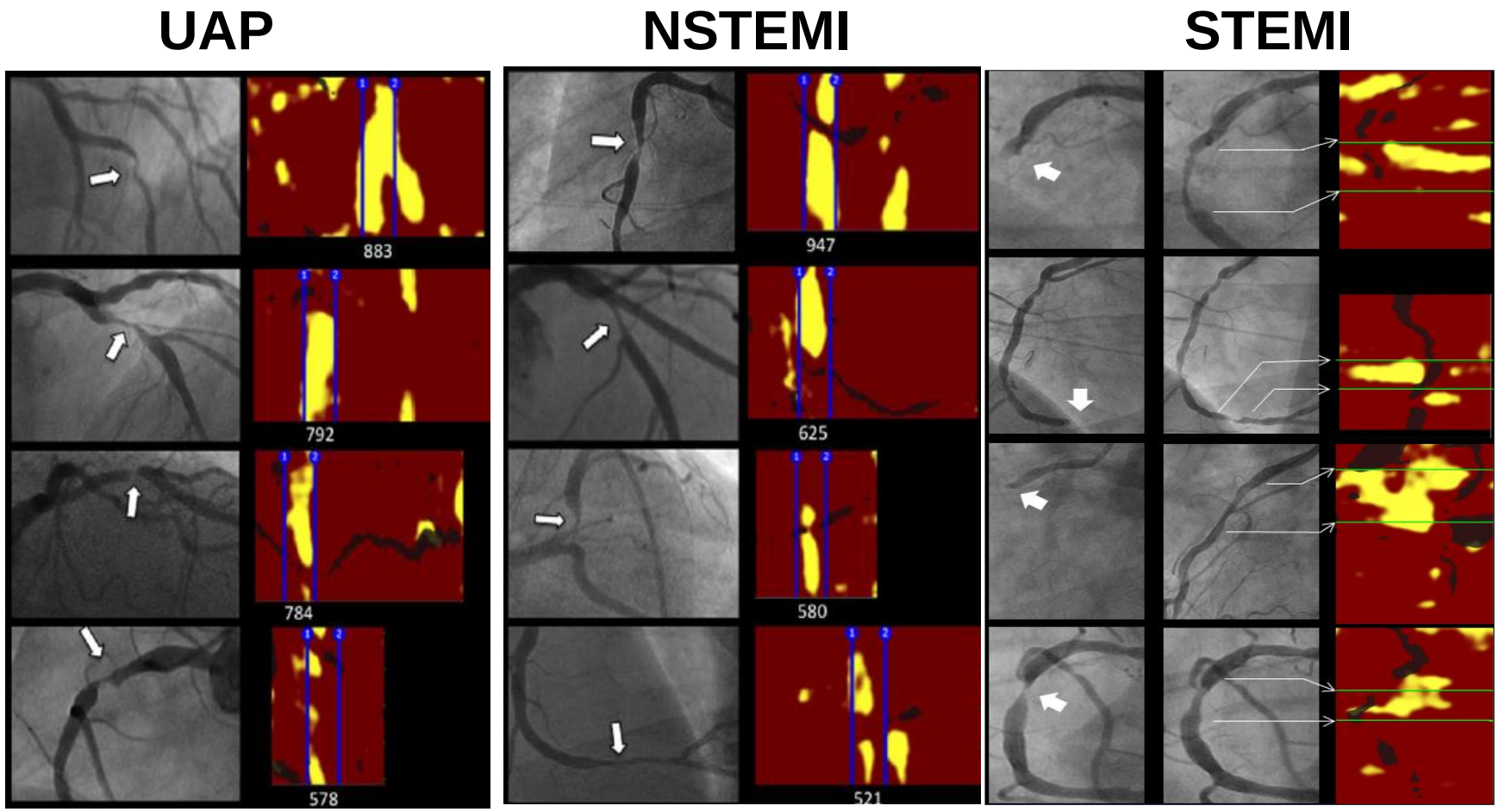
	HR [95% CI]	P value
PB_{MLA} ≥70%	5.03 [2.51, 10.11]	<0.0001
VH-TCFA	3.35 [1.77, 6.36]	0.0002
MLA ≤4.0 mm^2	3.21 [1.61, 6.42]	0.001

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

Adding
Lipid Core Burden Index

Lipid Core Burden

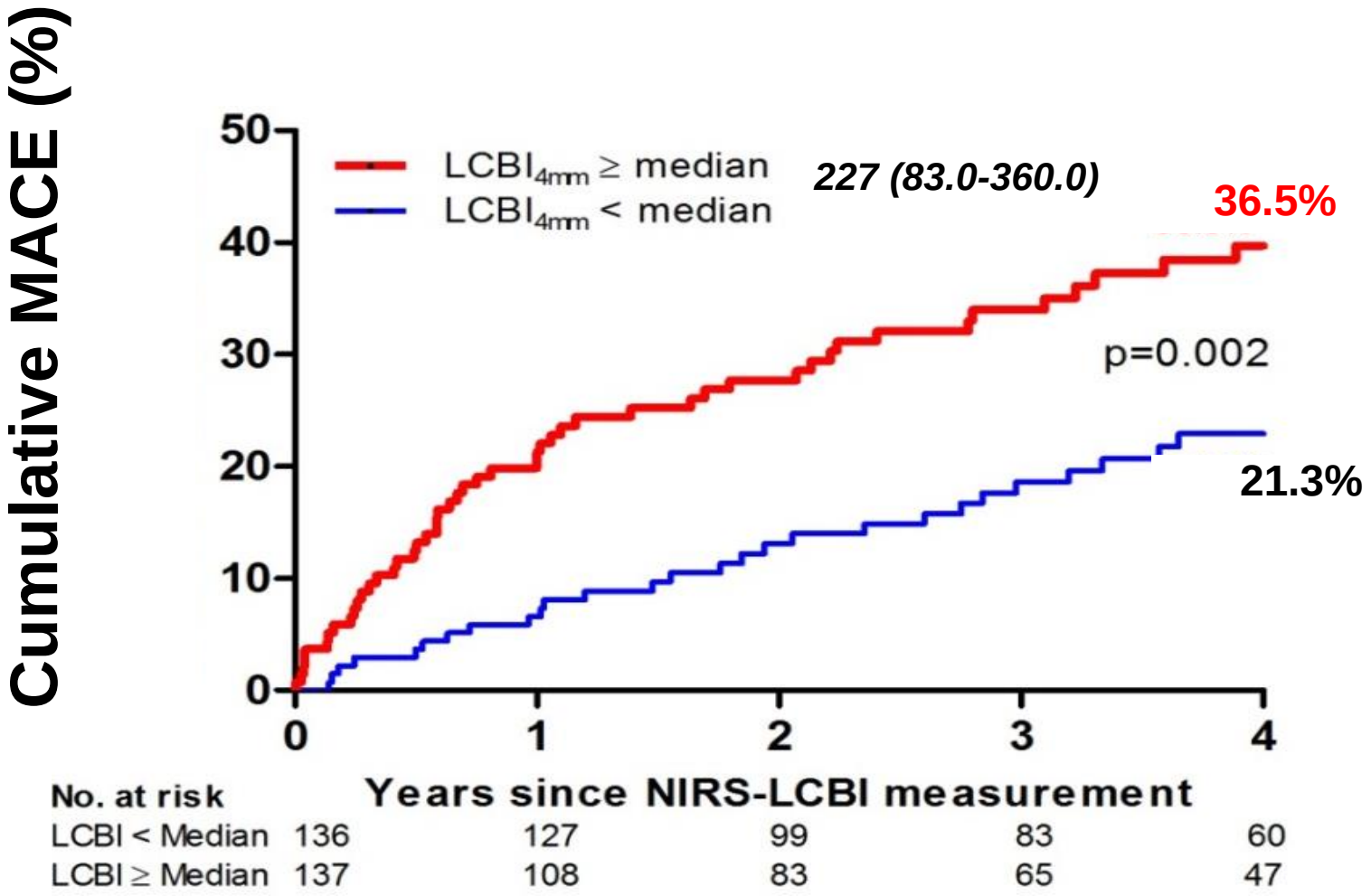
Near-infrared spectroscopy (NIRS)



Madder RD, Erlige, JACC Interv 2013, Cather Cardiovasc Interv 2015, Euro Atheroscl Soc 2013

Lipid Core Burden Index (LCBI)

Predicts MACE !



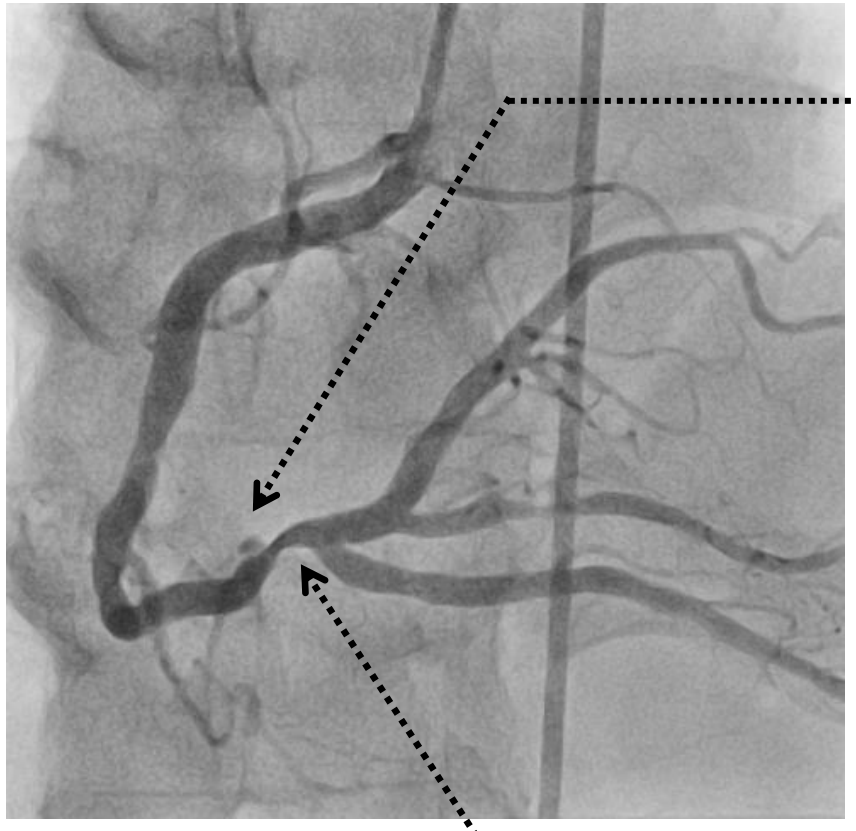
Schuurman et al. *European Heart Journal*, Volume 39, Issue 4, 21 January 2018, Pages 295–302

Imaging Definition of Vulnerable Plaque

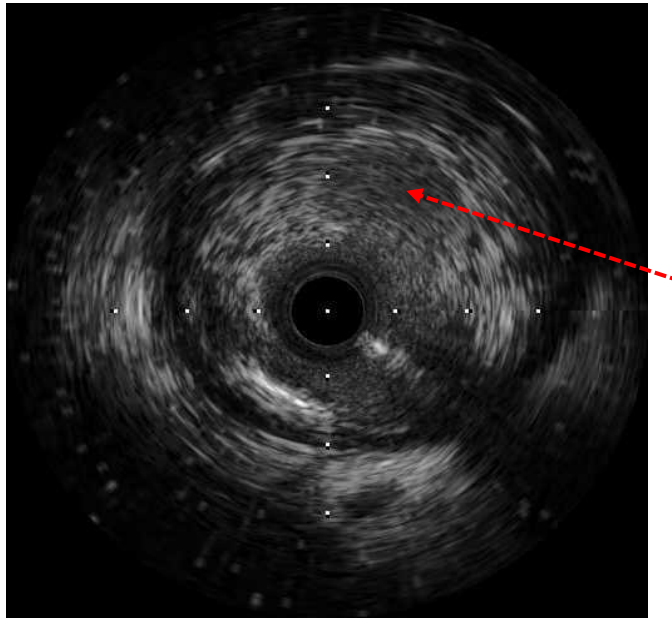
1. PB ≥70%
2. TCFA by OCT or VH-IVUS
3. MLA ≤4.0 mm^2
4. LRP on NIRS ($_{max}LCBI_{4mm}$>315)

Image Defined
Vulnerable Plaque

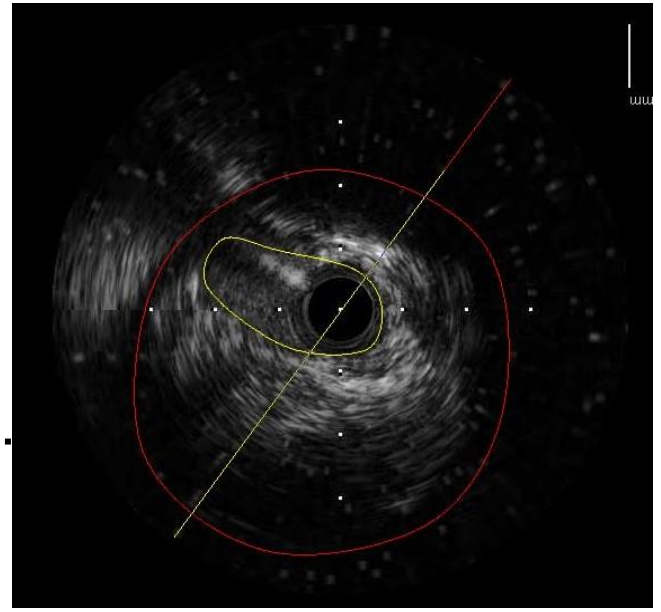
IVUS



FFR 0.89



Plaque Rupture

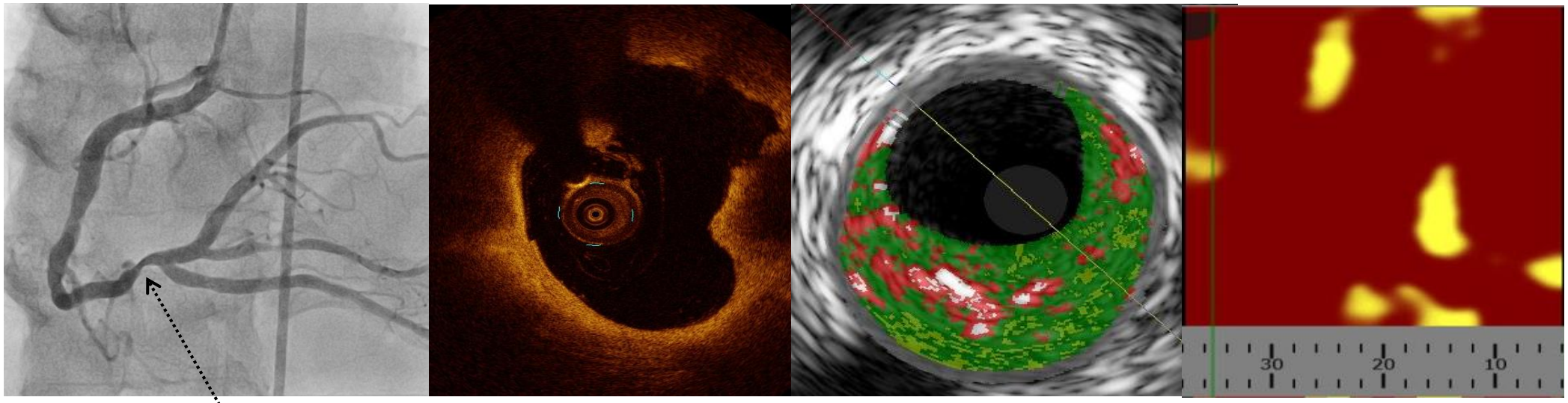


MLA:3.45 mm^2
Plaque burden 73 %

Vulnerable Plaque
by OCT, VH-IVUS & NIRS

Rupture, TCFA

$_{max}LCBI_{4mm}$= 404

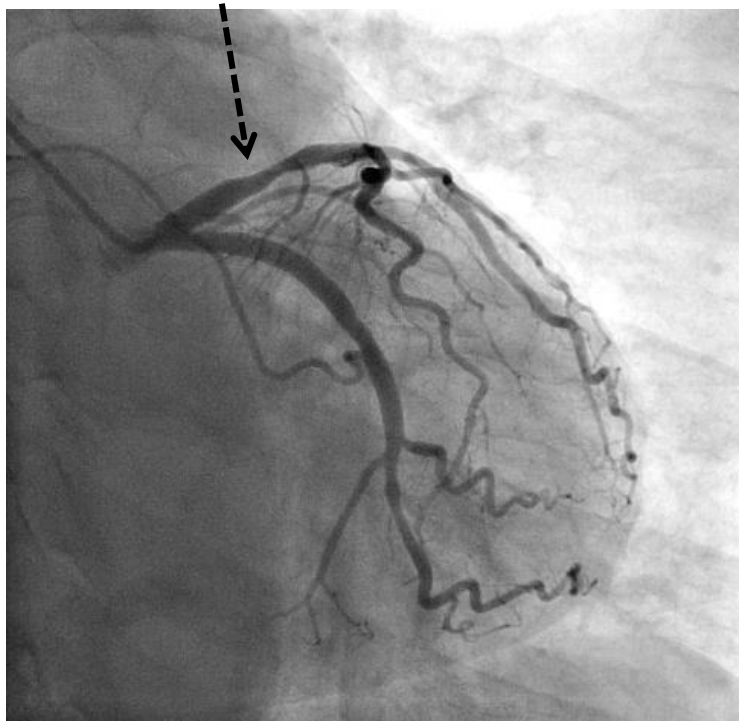


Necrotic Core 25%

FFR 0.89

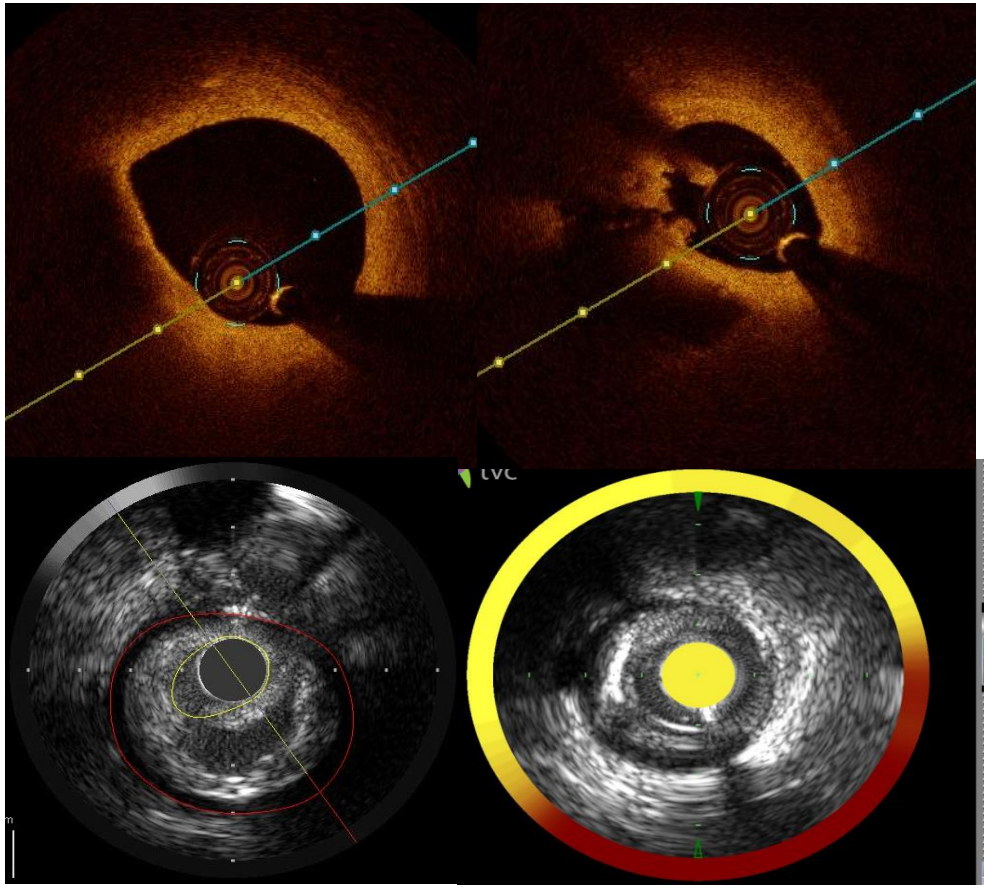
Vulnerable Plaque by OCT & NIRS

FFR 0.85



TCFA

Rupture & thrombi



MLA 2.7 mm^2
Plaque burden 73%

maxLCBI 4mm : 571

Treatment of the Vulnerable Plaque ??

Current strategies for the management of vulnerable plaques include lifestyle modifications, medication (e.g., statins, antiplatelet therapy), and invasive procedures (e.g., angioplasty, stenting, or bypass surgery) if necessary.

Question 1,

Can Optimal Medical Treatment Stabilize Plaque Vulnerability ?

STABLE Trial

(*ST*atin and *A*theroma Vulnera*B*i*L*ity *E*valuation)
Double-blinded, Prospective, Randomized, Controlled Trial

290 patients with
Deferred native coronary artery lesion

2:1 randomization, double-blinded

Rosuvastatin 40mg

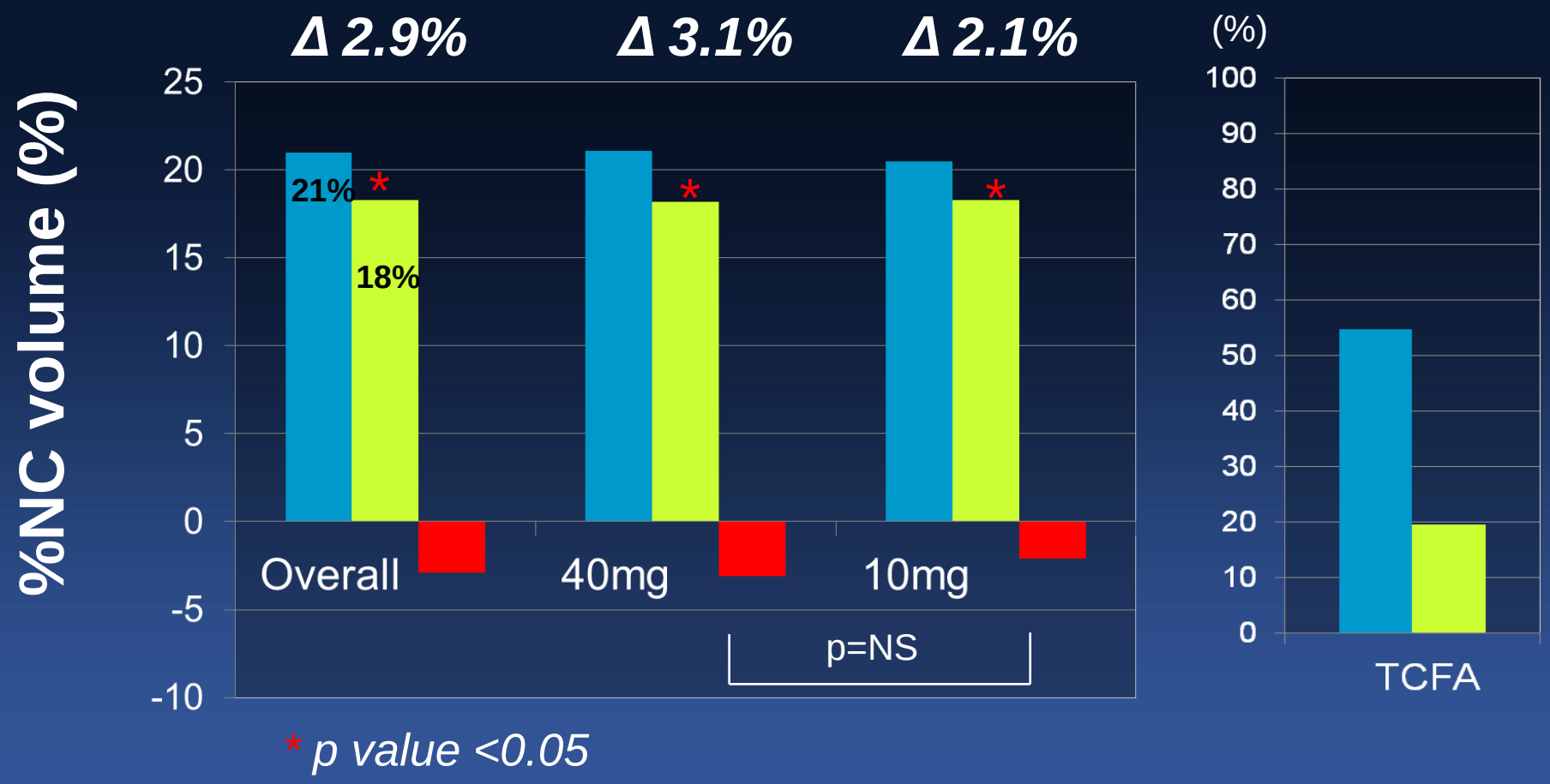
Rosuvastatin 10mg

Primary efficacy endpoint; Change in %NC volume within target segment by VH-IVUS at 1 year

Secondary endpoint: change in %NC volume comparing rosuvastatin 40mg vs. 10mg.

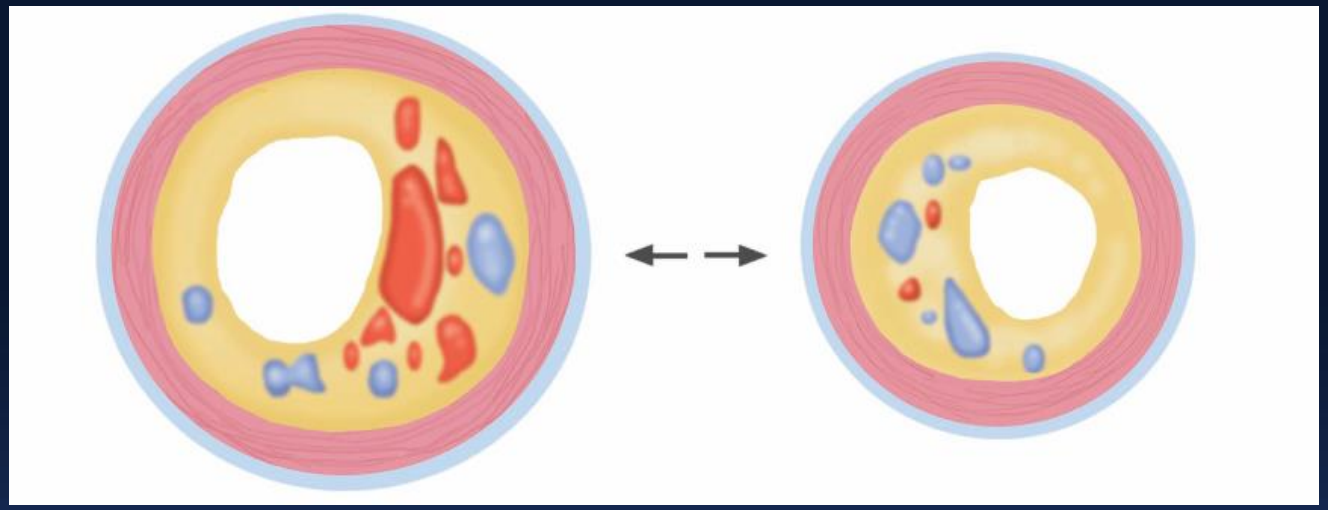
Park SJ, Kang SJ et al, JACC 2016;67(15):1772-1783

Primary Endpoint
%NC Volume Changes at 1 Year



* *p value <0.05*

Park SJ, Kang SJ et al, JACC 2016;67(15):1772-1783



Rosuvastatin Therapy Can Make A Plaque Regression and Stabilization at 1 year.

Park SJ, Kang SJ et al, JACC 2016;67(15):1772-1783

Treatment of the Vulnerable Plaque

Conservative management strategies: Lifestyle modifications and optimal medical therapy (OMT), including statins, antiplatelet agents, and antihypertensive medications, can stabilize vulnerable plaques and reduce the risk of rupture. These approaches should be considered and optimized before deciding on an invasive procedure like stenting.

ChatGPT4

Question 2,

Can PCI Stabilize

Plaque Vulnerability ?

Treatment of the Vulnerable Plaque ?

Stenting for vulnerable plaques is a complex and debated topic among medical professionals.

Stenting a vulnerable plaque could potentially prevent plaque rupture and the subsequent risk of a heart attack or stroke. However, there are several factors to consider before deciding on stenting for a vulnerable plaque:

Treatment of the Vulnerable Plaque

1. Risk of procedural complications: These risks should be weighed against the potential benefits of the procedure.

2. Lack of reliable identification methods: Although advanced imaging techniques like intravascular ultrasound (IVUS) and optical coherence tomography (OCT) can help identify vulnerable plaques, it can still be challenging to accurately predict which plaques are at the highest risk of causing future events.

Treatment of the Vulnerable Plaque

3. Conservative management strategies: Lifestyle modifications and optimal medical therapy (OMT), including statins, antiplatelet agents, and antihypertensive medications, can stabilize vulnerable plaques and reduce the risk of rupture. These approaches should be considered and optimized before deciding on an invasive procedure like stenting.

Treatment of the Vulnerable Plaque

4. Incomplete understanding of vulnerable plaque progression: The natural history of vulnerable plaques is not yet fully understood. Some vulnerable plaques may stabilize over time, while others may progress to cause a cardiovascular event. This makes it difficult to determine when stenting would be most beneficial.

Treatment of the Vulnerable Plaque

In summary, stenting for vulnerable plaques is a controversial topic. It is essential to weigh the potential benefits against the risks and consider conservative management strategies before opting for an invasive procedure.

PROSPECT ABSORB RCT

≥1 non-flow-limiting NCL with site-assessed ≥65% plaque burden (n=182)

R 1:1

92 received allocated intervention
1 DES implanted instead of BVS
Analyzable IVUS (n=91)

ABSORB BVS + GDMT (N=93)

GDMT alone (N=89)

88 received allocated intervention
1 Absorb BVS implanted in error
Analyzable IVUS (n=88)

Routine angiography with 3V IVUS-NIRS FU at 25 months

Clinical follow-up at 24 months (n=93)	Clinical follow-up at 24 months (n=88)
Follow-up angiography (n=87)	Follow-up angiography (n=80)
Qualifying follow-up IVUS (n=85)	Qualifying follow-up IVUS (n=77)
Analyzable follow-up IVUS (n=84)	Analyzable follow-up IVUS (n=72)
Analyzable baseline and follow-up IVUS (n=83)	Analyzable baseline and follow-up IVUS (n=72)

2-year clinical FU 181 pts (99.5%); median clinical FU 4.1 years
25-mo angio FU 167 pts (91.8%); qualifying IVUS FU 156 pts (85.7%)

Gregg Stone et al, J Am Coll Cardiol. 2020 Nov 17;76(20):2289-2301.

Baseline Core Lab Imaging

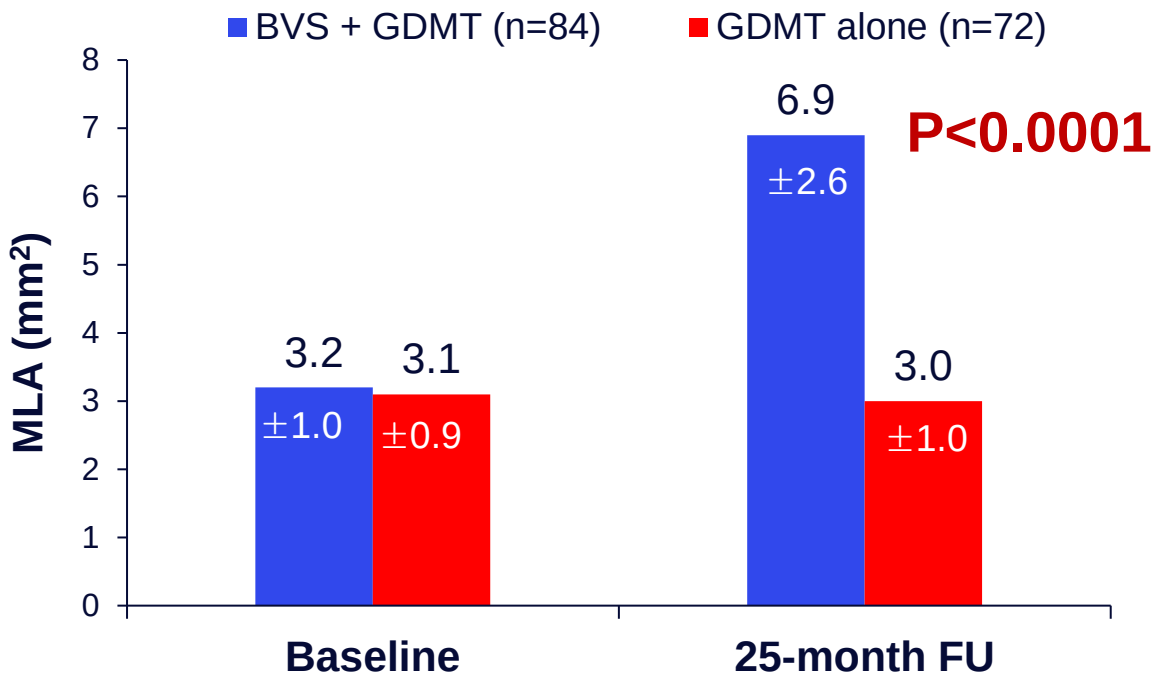
- 182 patients and lesions randomized -

Baseline feature	BVS plus GDMT (N=93)	GDMT alone (N=89)
High-risk Plaque Morphology		
Lesions with plaque burden ≥70%	76.1% (70/92)	78.4% (69/88)
Lesions with $maxLCBI_{4mm}$ ≥324.7*	51.7% (46/89)	53.5% (46/86)
Lesions with MLA ≤4.0 mm^2	78.3% (72/92)	88.6% (78/88)
Lesions with ≥1 of 3 high-risk plaque characteristics†	93.3% (83/89)	97.7% (84/86)
Lesions with ≥2 of 3 high-risk plaque characteristics†	71.9% (64/89)	76.7% (66/86)
Lesions with 3 of 3 high-risk plaque characteristics†	40.4% (36/89)	45.3% (39/86)

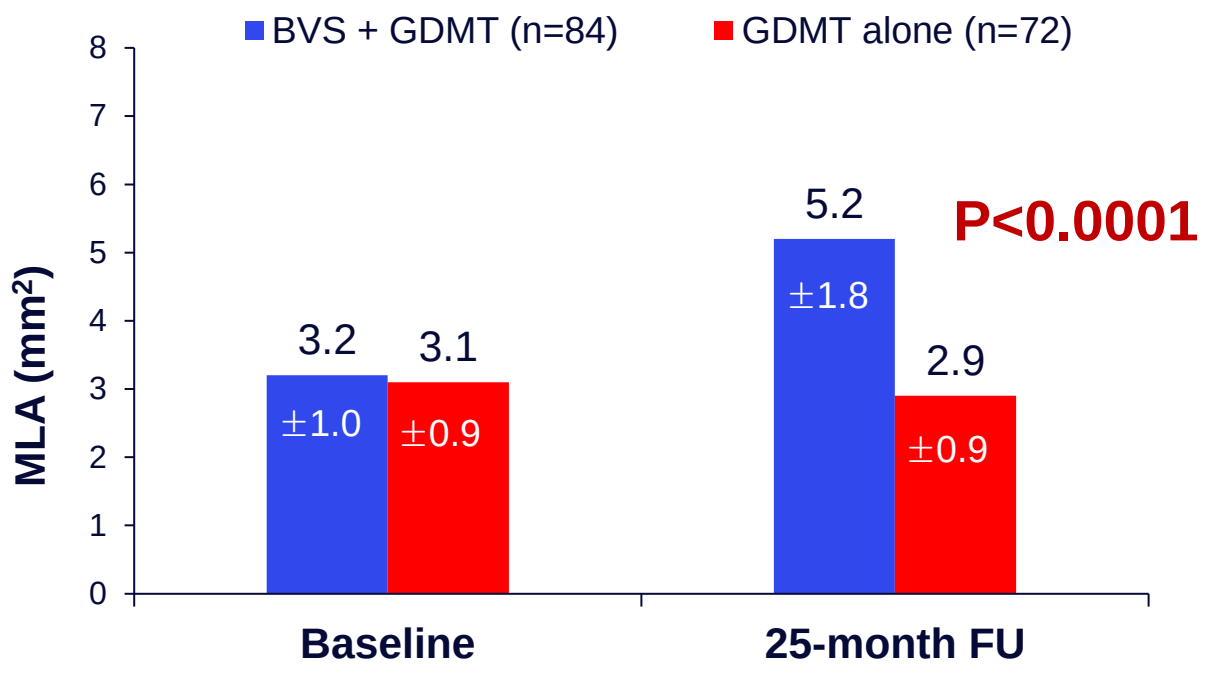
IVUS MLA at 25-Month f/u

Primary Powered Endpoint

At the original MLA site (primary analysis)



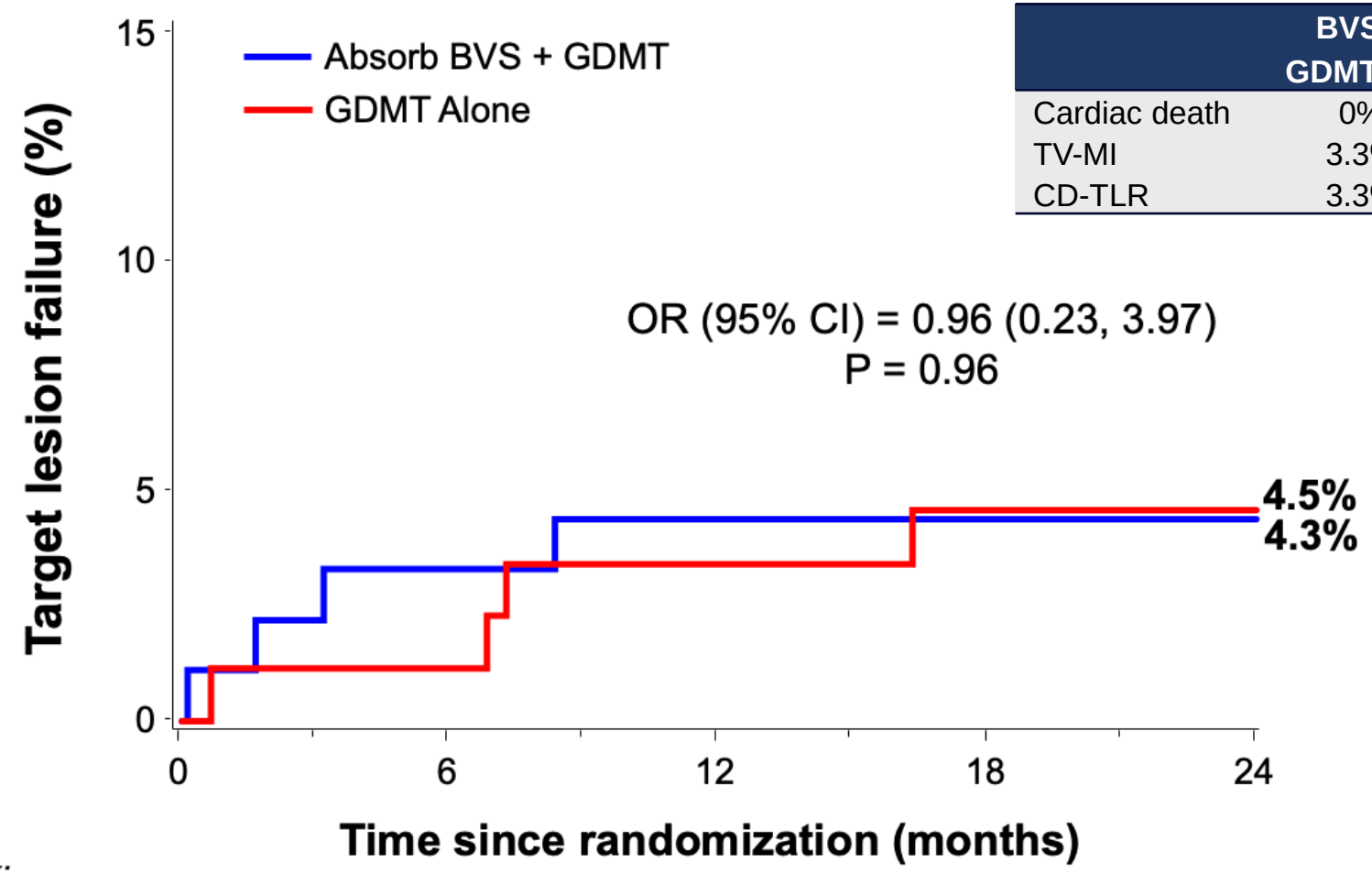
Across the entire lesion (includes 5 mm margins)



J Am Coll Cardiol. 2020 Nov 17;76(20):2289-2301.

Target Lesion Failure at 24 Months

	BVS plus GDMT (N=92)	GDMT alone (N=89)
Cardiac death	0% (0)	0% (0)
TV-MI	3.3% (3)	1.1% (1)
CD-TLR	3.3% (3)	3.4% (3)

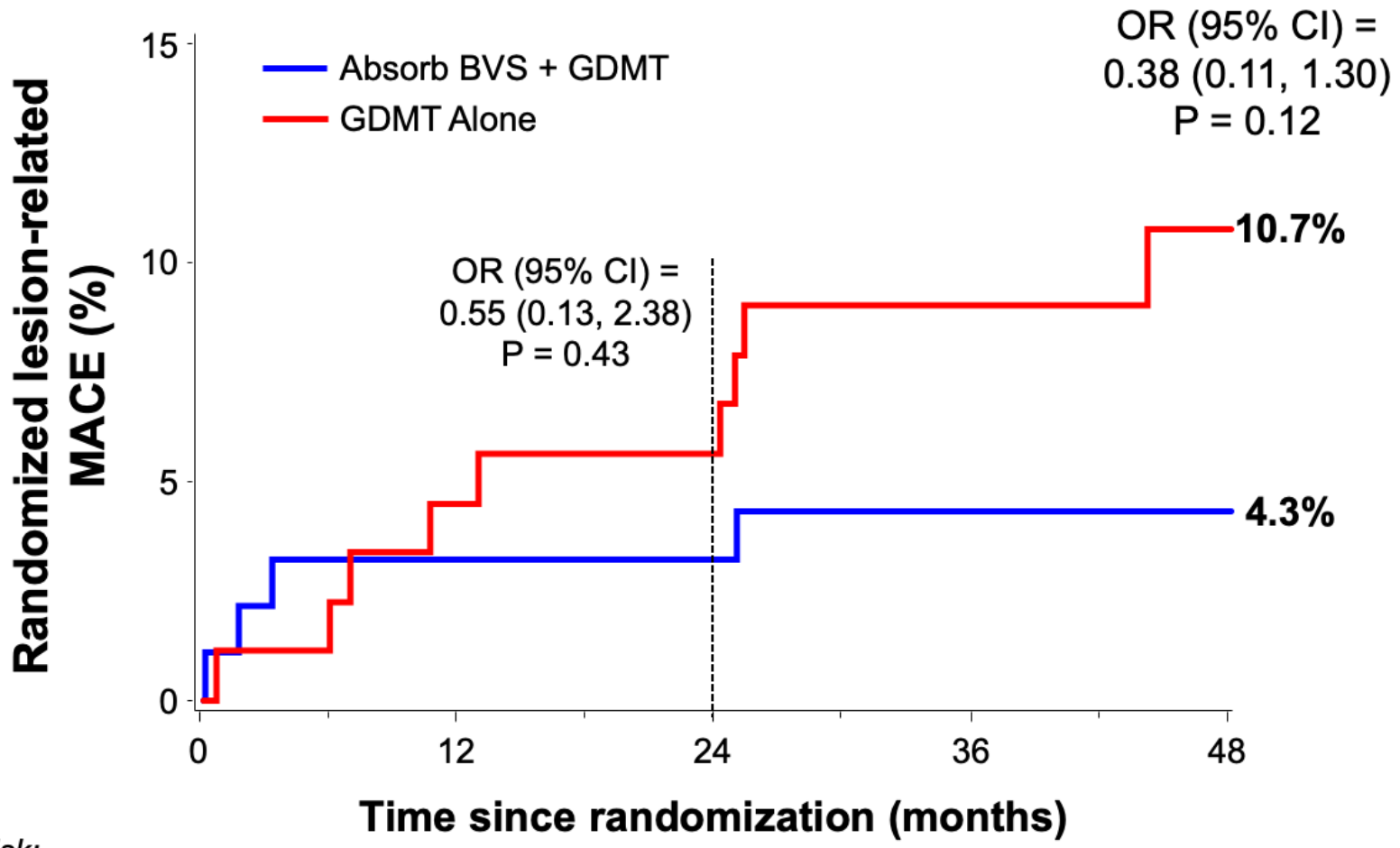


Number at risk:

Absorb BVS + GDMT	92	89	88	88	88
GDMT Alone	89	88	86	84	84

Lesion-Related MACE

(cardiac death, MI, unstable angina, or progressive angina)



Number at risk:

Absorb BVS + GDMT	93	90	90	78	45
GDMT Alone	89	85	83	68	42

Lesion-Related MACE

Event rate, entire study	BVS plus GDMT (N=93)	GDMT alone (N=89)	P value
MACE	4.3% (4)	10.7% (9)	0.12
- Cardiac death	0% (0)	0% (0)	-
- Myocardial infarction	2.2% (2)	1.7% (1)	-
- Procedural	0% (0)	0% (0)	-
- Non-procedural	2.2% (2)	1.7% (1)	-
- Unstable angina	1.1% (1)	0% (0)	-
- Progressive angina	1.1% (1)	9.0% (8)	-
- Requiring revascularization	1.1% (1)	6.8% (6)	-
- With ACL-confirmed rapid lesion progression	0% (0)	2.2% (2)	-
Clinically-driven revascularization	4.3% (4)	8.5% (7)	-
- PCI	4.3% (4)	8.5% (7)	-
- CABG	0% (0)	0% (0)	-
Scaffold thrombosis*	1.1% (1)	-	-

*Thrombosis at day 50 of a Dg side-branch pinched by LAD BVS struts, w/o scaffold thrombosis

J Am Coll Cardiol. 2020 Nov 17;76(20):2289-2301.

Ultimate Question,

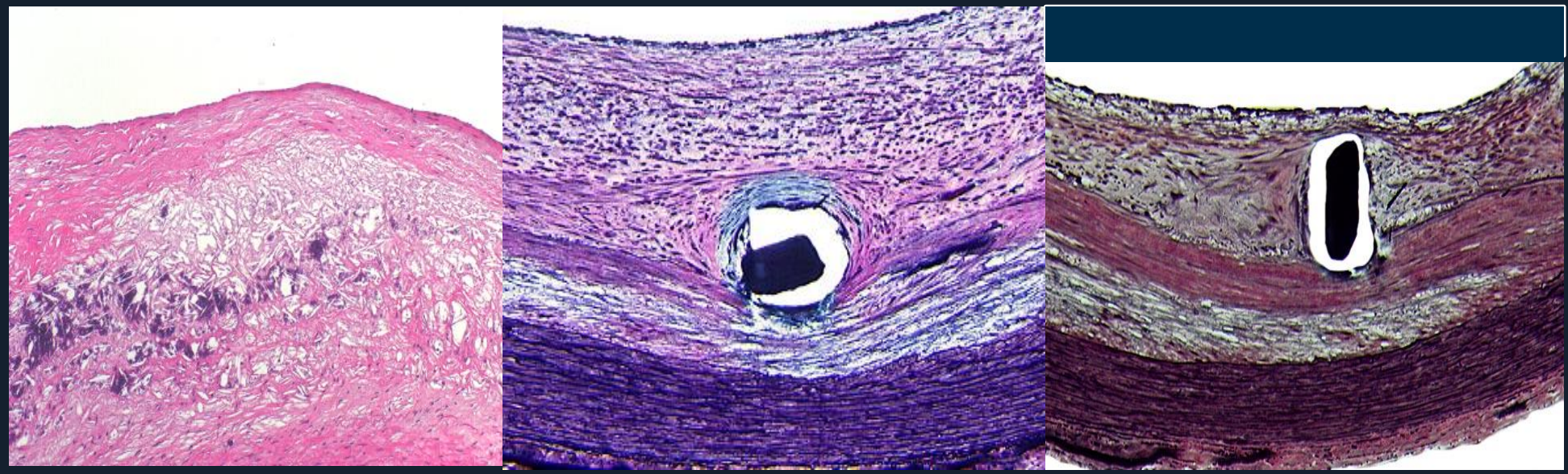
Which One Would Be Better ?
PCI vs. Optimal Medical Treatment.

PREVENT Study,

The ***PREVENT***ive Implantation of BVS or DES Compared to Optimal Medical treatment on Stenosis With Functionally Insignificant Vulnerable Plaque.

Background

Everolimus(BVS or Xience) Induced Less Neointimal Hyperplasia on TCFA



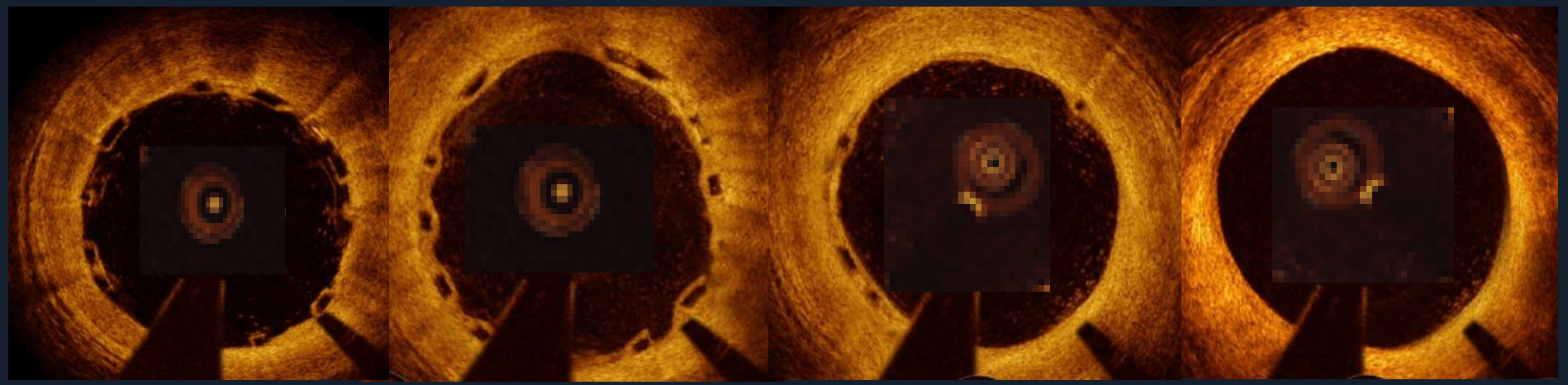
TCFA

Metallic & Polymer Strut

Everolimus Strut

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

BVS Suggested
Plaque Stabilization and Lumen Enlargement



1 month | 6 month | 2 year | 5 year

PREVENT Trial

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

1. TCFA by OCT or VH-IVUS
2. IVUS MLA ≤4.0mm^2
3. IVUS Plaque Burden >70%
4. Lipid-Rich Plaque on NIRS ($_{max}LCBI_{4mm}$>315)

R

BVS or DES +OMT
N=800

OMT
N=800

Primary endpoint :*Target Vessel Failure at 2 years*
(A Composite of CV death, MI, Target Vessel Revascularization, or Unplanned Hospitalization for Angina adjudicated to Target Vessel)

Objective,

To determine whether BVS or DES (Xience Stent) 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 1,600 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 or VH-IVUS
2. IVUS MLA<4mm2
3. IVUS plaque burden>70%
4. Lipid-rich plaque on NIRS ($_{max}LCBI_{4mm}$>315)

Exclusion Criteria

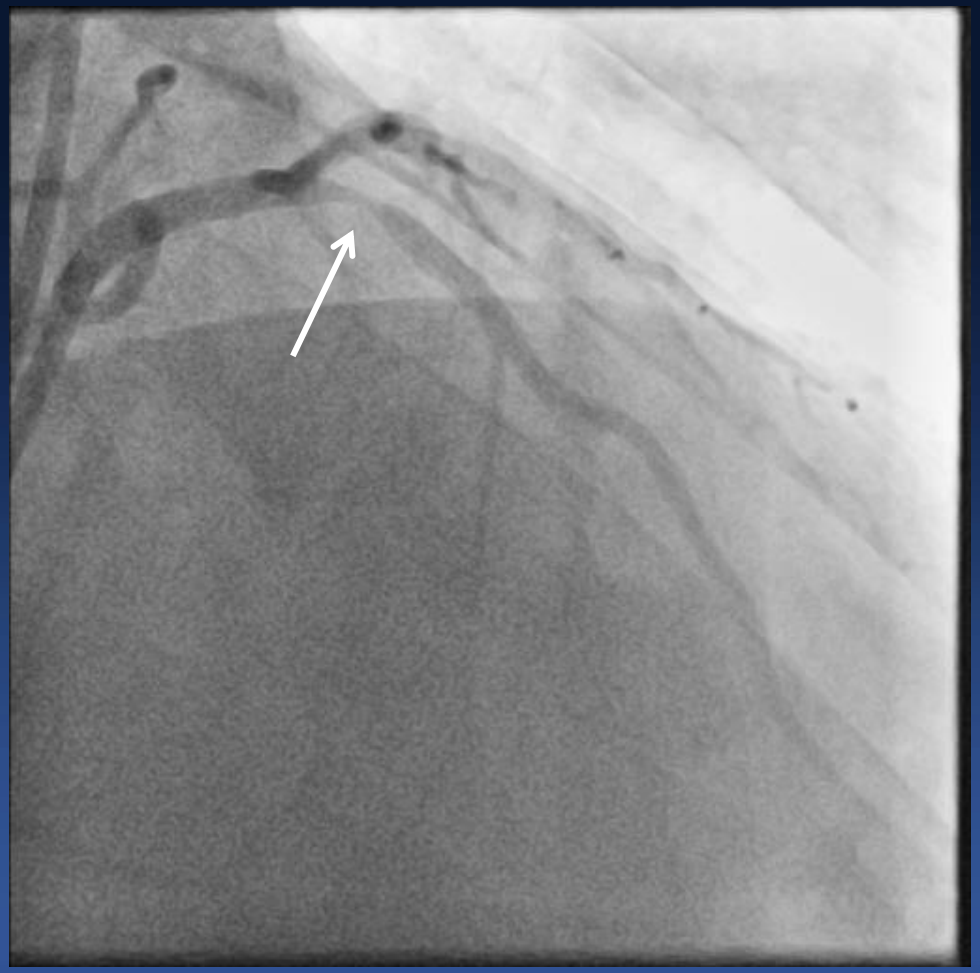
Contraindication to dual antiplatelet therapy, Life expectancy <2y, Planned cardiac surgery or planned major non cardiac surgery, Preferred treatment for CABG, STEMI, Bypass graft lesion, Woman who are breastfeeding, pregnant or planning to become pregnant during the course of the study.

Primary and Major Secondary End Point,

The primary endpoint: ***<u>Target Vessel Failure at 2 years</u>***
(A Composite of CV death, MI, Target Vessel Revascularization, or Unplanned Hospitalization for Angina adjudicated to Target Vessel)

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

BVS Arm



Angiographic DS : 80%

FFR : 0.83

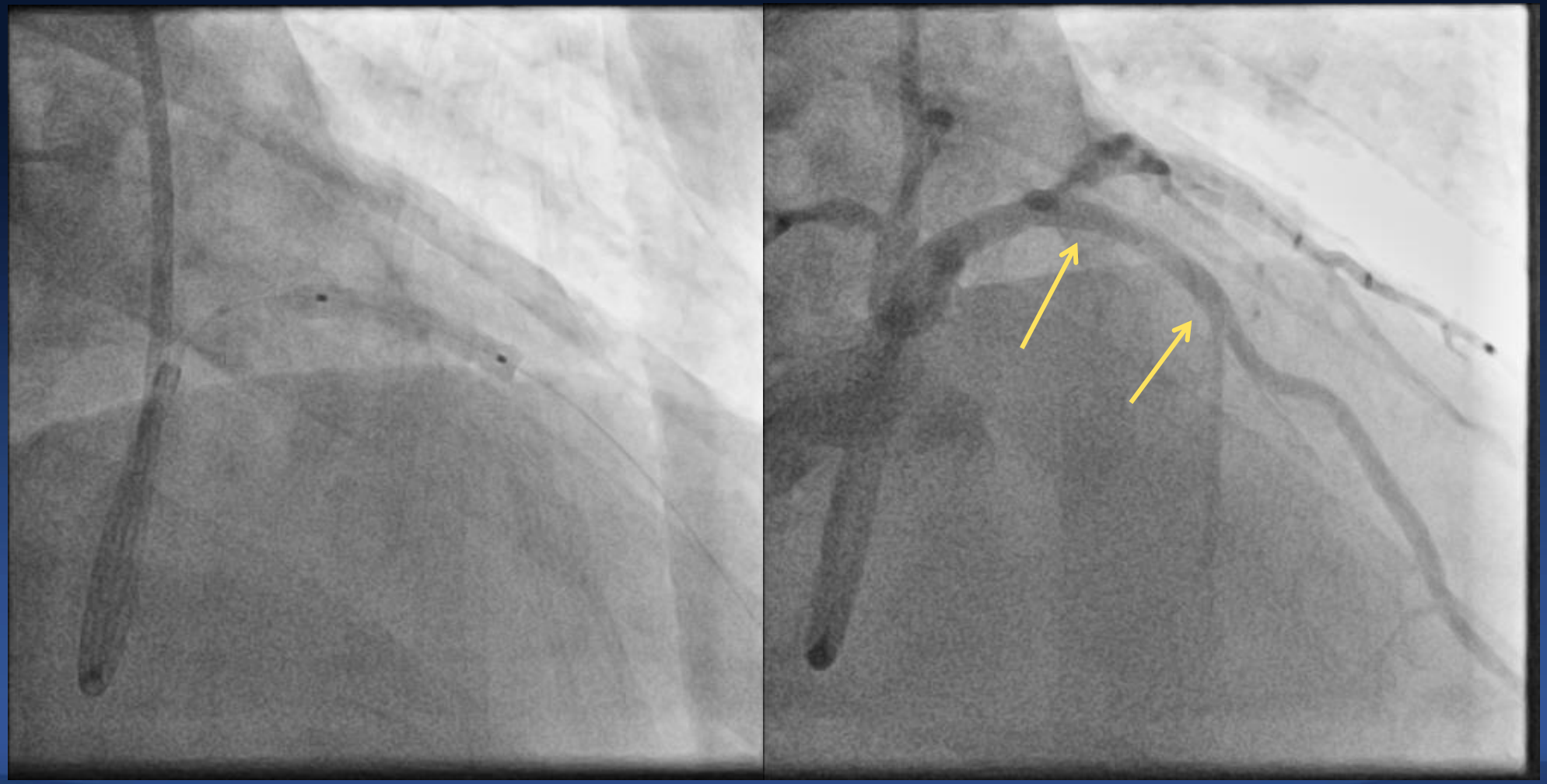
IVUS MLA : 2.11 mm²

Plaque burden : 77%

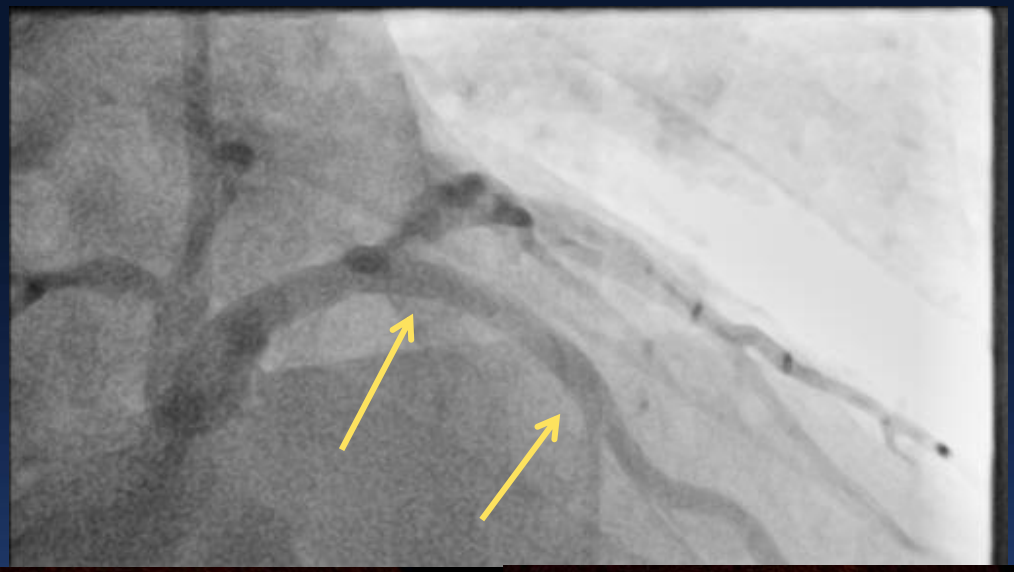
$_{max}LCBI_{4mm}$: 93

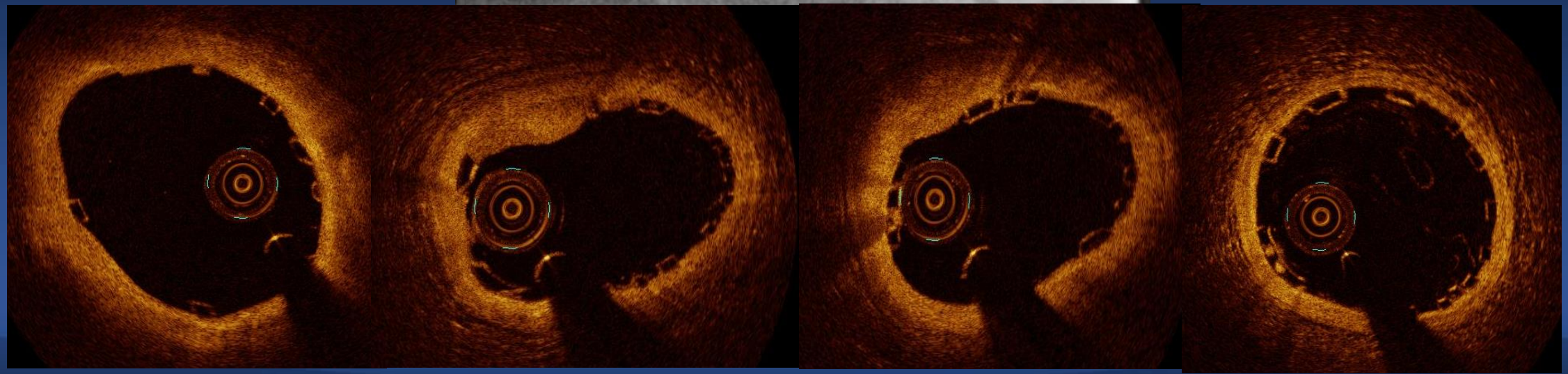
Necrotic core : 15%

Absorb (BVS)
3.5 mm x 18 mm



Post PCI - OCT





PREVENT Trial,

8 Countries, 33 Centers

Principal Investigators, Seung-Jung Park, MD, PhD. Korea
Co-PI, Duk-Woo Park, Gregg Stone

Columbia University Medical Center	Gregg Stone
Asan Medical Center	Seung-Jung Park
Gachon University Gil Hospital	Tae hoon Ahn
The Catholic University of Korea, Daejeon ST. Mary's Hospital	Sung-Ho Her
The Catholic University of Korea Seoul St. Mary's Hospital	Ki-Yuk Chang
Kangwon National University Hospital	Bong-Ki Lee
Keimyung University Dongsan Medical Center	Chang Wook Nam
Korea University Guro Hospital	Seung Un Na
Daegu Catholic University Medical Center	Kee-Sik Kim
Seoul National University Bundang hospital	In-Ho Chae
Seoul National University hospital	Bon-Kwon Koo
Ulsan University Hospital	Eun-Seok Shin
Chonnam National University Hospital	Young-Keun Ahn

ChonBuk National University Hospital	Jei Keon Chae
Chungnam National University Hospital	Si Wan Choi
Hallym University Sacred Heart Hospital	Hyun Sook Kim
Bundang Cha Medical Center	Won-Jang Kim
Inje University Busan Paik Hospital	Tae Hyun Yang
Samsung Medical Center	Joo-Yong Hahn
Prince of Wales Hospital	Nigel Jepson
Queen Elizabeth Hospital	Michael Kang-Yin Lee
San Raffaele Hospital, Italy	Antonio Colombo
Aichi Medical University	Tetsuya Amano
Kawasaki Medical School	Shiro Uemura
Kyoto University Hospital	Takeshi Kimura
Wakayama Medical University	Takashi Akasaka
Christchurch Hospital	David Smyth
National Taiwan University hospital	Paul Hsien-Li Kao
Saint Luke's Mid America Heart Institute	David J. Cohen
Stanford University Medical Center	Alan C. Yeung
Washington Hospital Center	Ron Waksman

PCI for Vulnerable Plaque ?

New Paradigm ?

We Will Have An Answer in ACC 2024 !