PROSPECT II: A Prospective Natural History Study Using NIRS-IVUS Imaging in Patients with Acute Myocardial Infarction

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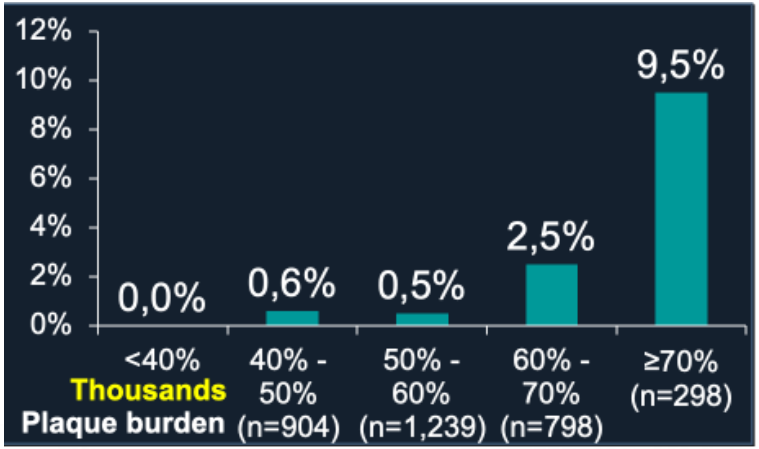
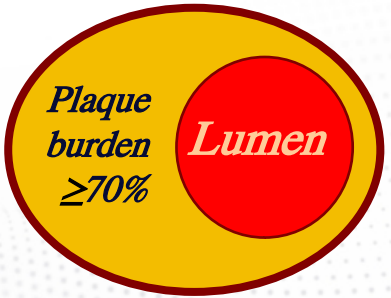
Disclosures

- In the past 12 months David Erlinge has received Speakers fees – Amgen, AstraZeneca, Bayer, Chiesi and fees for Advisory boards – Bayer, Boehringer-Ingelheim, Sanofi.

Background

- ACS most often arise from disruption and thrombosis of lipid-rich atherosclerotic plaques
- Identification of such "vulnerable" plaques before they progress may enable pre-emptive pharmacologic or other strategies to stabilize the plaque, prevent atherosclerosis progression and improve outcomes
- In the PROSPECT study, a large plaque burden, small lumen area and VH-TCFA assessed by intravascular ultrasound (IVUS) identified angiographically mild lesions at increased risk to cause future adverse events

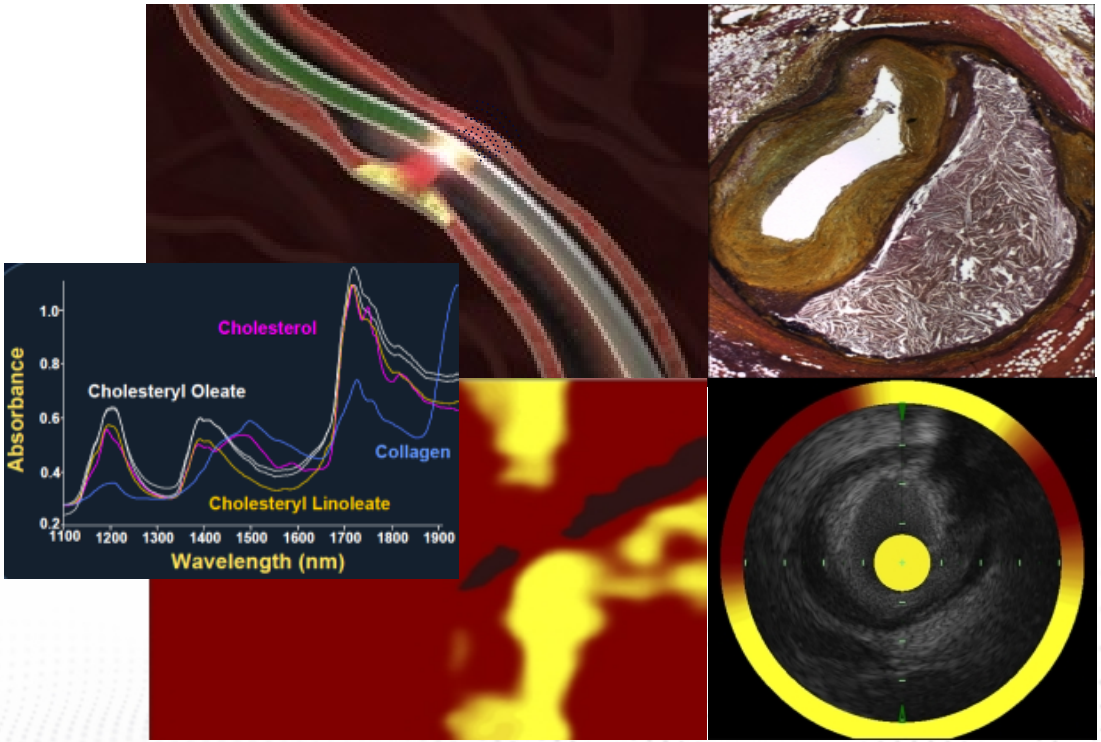




Stone GW et al. NEJM 2011;364:226-35
McPherson JA et al. JACC Img 2012;5:S76–85

Lipid-rich Core and NIRS

- Plaques causing MI and sudden cardiac death commonly contain a lipid-rich core
- Lipid content can be quantified by **near-infrared spectroscopy** (**NIRS**) in human coronary arteries (FDA approved)
- Retrospective reports and a recent prospective study have suggested that lipid-rich plaques detected by intracoronary NIRS imaging are associated with adverse **outcomes**



[1]Virmani R et al. ATVB 2000;20:1262-75
[2]Madder RD et al. ATVB 2016;36:1010-5
[3]Waksman R et al. Lancet 2019;394:1629-37

PROSPECT II: Design

- After successful treatment of all flow-limiting lesions in pts with recent MI (STEMI or troponin + NSTEMI), intravascular imaging was performed in the proximal 6-10 cm of all 3 coronary arteries with a combination NIRS-IVUS catheter
- Untreated "non-culprit" lesions (NCLs) were prospectively identified by IVUS and their lipid content was assessed by blinded NIRS
- Based on follow-up angiography, adverse cardiovascular events were classified as attributable to:
  - Originally-treated culprit lesions
  - Scaffold-randomized treated lesions
  - Untreated non-culprit lesions (NCLs)
  - Indeterminate (no follow-up angiography)

PROSPECT II: Design, cont

- The primary outcome was MACE during long-term follow-up, the composite of cardiac death, MI, unstable angina or progressive angina either requiring revascularization or with rapid lesion progression, attributed to originally untreated NCLs

- A RCT, PROSPECT ABSORB, was embedded in PROSPECT II

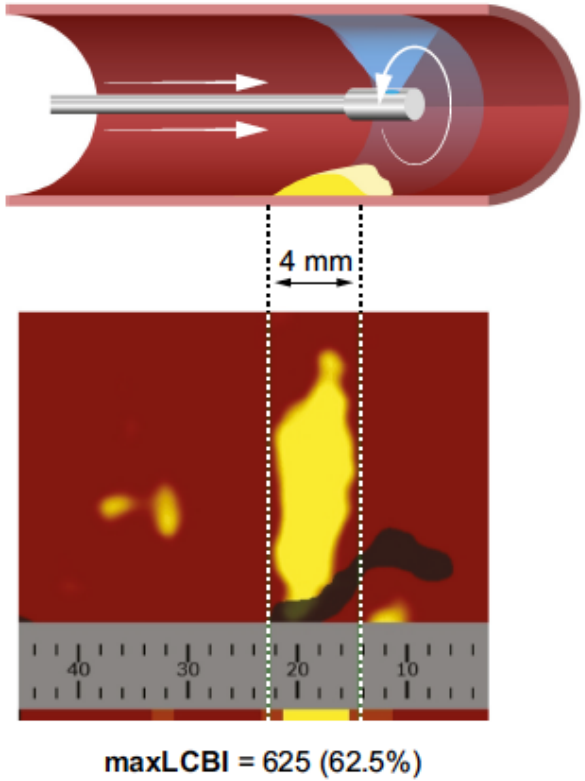
  - Angiographically non-obstructive lesions with IVUS plaque burden ≥65% were randomized to treatment with BVS plus guideline-directed medical therapy (GDMT) versus GDMT alone

  - Randomized lesions treated with a scaffold were excluded from the PROSPECT II natural history analysis

Imaging Analysis
Angiography and IVUS

- Angiograms and intravascular images were prospectively analyzed at an independent core laboratory (CRF) without knowledge of patient outcomes
- Angiographic analyses were performed of all lesions with ≥30% DS in each epicardial vessel and sidebranch ≥1.5 mm in diameter using an automated edge-detection algorithm
- IVUS evaluation of all image cross-sections and quantitative measurements every mm were performed
- Culprit lesions were defined by IVUS as the treated segment including 5 mm proximal and distal stent edges
- NCLs were defined as untreated coronary segments ≥2 mm in length with ≥40% plaque burden

Imaging Analysis: NIRS



- NIRS spectroscopic data generates a chemogram, a color-coded distribution of lipid probability with the x-axis corresponding to the axial vessel position (0.1 mm/pixel) and the y-axis corresponding to the circumferential position (1°/pixel)
- Low probability of lipid is shown as red and high probability of lipid is shown as yellow
- Lipid core burden index (LCBI) = the fraction of pixels with probability of lipid >0.6 divided by all analyzable pixels within the region of interest, multiplied by 1000
- $MaxLCBI_{4mm}$ = the maximum LCBI within any 4 mm segment across the entire lesion

Statistical Analysis

- The principal study objective was to establish the covariate-adjusted relationship between high-risk characteristics of untreated NCLs and subsequent patient-level (1°) and lesion-level (2°) outcomes
- High-risk untreated plaque characteristics were pre-specified as:
  - Lipid-rich plaque (defined as the upper quartile of maxLCBI $_{4mm}$ of all NCLs)
  - Maximum plaque burden (PB) ≥70%
  - Minimum lumen area (MLA) ≤4.0 mm ^{2}
- Each individual high-risk plaque characteristic was introduced in a separate multivariable model in a hierarchical order (LRP followed by PB followed by MLA) to account for multiplicity

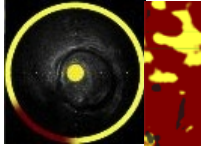
PROSPECT II Organization, Leadership, Committees and Core Laboratories

- Coordinating PIs and Study Chairmen: David Erlinge and Gregg W. Stone
- AROs: CRF (Ori-Ben-Yehuda, Executive Director) and UCR (Jonas Oldgren, Executive Director)
- Sponsor, Project and Data Management : UCR, Frida Kåver (Project Manager), Lars Wallentin (sponsor representative)
- Clinical Events Committee: UCR, Claes Held (Chair)
- Angiographic Core Lab: CRF, Ziad A. Ali (Director)
- IVUS-NIRS Core Lab: CRF, Akiko Maehara (Director)
- Programming, Biostatistics and Data Analysis: CRF, Aaron Crowley (Director)
- DSMB: Patrick W. Serruys (Chair)
- Funding support: Abbott Vascular, Infraredx Inc, The Medicines Company

PROSPECT II
PROSPECT ABSORB

PROSPECT II Natural History Study

PROSPECT ABSORB RCT



902 pts with troponin + ACS after successful PCI enrolled at 16 centers

3 vessel IVUS + NIRS (blinded)

4 pts were not followed beyond 30 days because NCL imaging data was not acquired; these pts remained in the safety cohort

898 pts: ≥1 non-flow limiting lesion with ≥65% plaque burden?

Yes (N=182)

No (n=716)

R 1:1

ABSORB BVS + GDMT (N=93)

GDMT (N=89)

Routine angio/3V IVUS-NIRS FU at 25 months

Clinical FU in PROSPECT II: Median 3.7 years

ClinicalTrials.gov
NCT02171065

PROSPECT II

Hospitals and Principal Investigators

- **Denmark (529 enrolled):** National Coordinating Investigator: Thomas Engstr øm.
  Aarhus: Hans Erik B øtker, Michael Maeng, Roskilde: Lars Kj øller-Hansen,
  Copenhagen: Thomas Engstr øm, Odense: Lisette Okkels Jensen

- **Sweden (261 enrolled):** National Coordinating Investigator: David Erlinge.
  Lund: David Erlinge, Örebro: Ole Fröbert, Danderyd Hospital, Stockholm: Jonas Persson, Gothenburg: Elmir Omerovic, Uppsala: Stefan James, Södersjukhuset, Stockholm: Ulf Jensen, Falun: Iwar Sjögren, Kalmar: Jörg Carlsson

- **Norway (112 enrolled):** National Coordinating Investigator: Jan Erik Nordrehaug.
  Trondheim: Rune Wiseth, Stavanger: Alf Inge Larsen, Bergen: Öyvind Bleie,
  Tromsö: Thor Trovik

Baseline Characteristics

- 898 patients* with recent MI -

Baseline feature		Clinical presentation	
Age (years)	63.0 (55.0, 70.0)	STEMI	22.2% (199/898)
Sex, female	17.0% (153/898)	NSTEMI	77.8% (699/898)
Current or recent smoker	31.8% (282/886)	BMI (kg/m^2)	27.1 (24.8, 30.3)
Diabetes mellitus	12.1% (109/898)	Total cholesterol (mg/dL)	201.1 (166.3, 228.2)
- Insulin-treated	4.1% (38/898)	- LDL (mg/dL)	127.6 (100.5, 154.7)
Prior PCI	11.9% (107/898)	- HDL (mg/dL)	42.5 (37.1, 54.1)
Prior MI	9.9% (89/896)	- TGs (mg/dL)	124.0 (84.1, 186.0)
Hypertension requiring medication	37.2% (334/898)	Hemoglobin A1c, %	5.6 (5.4, 6.0)
Hyperlipidemia requiring medication	25.2% (226/898)	Creatinine clearance* (mL/min)	99.2 (80.1, 120.9)
Prior stroke or TIA	5.2% (47/898)	High-sensitivity CRP (µg/mL)	3.4 (1.5, 6.1)

*Per protocol, 4 consented pts were not followed beyond 30 days because NCL imaging data was not acquired

Imaging Findings: NCLs

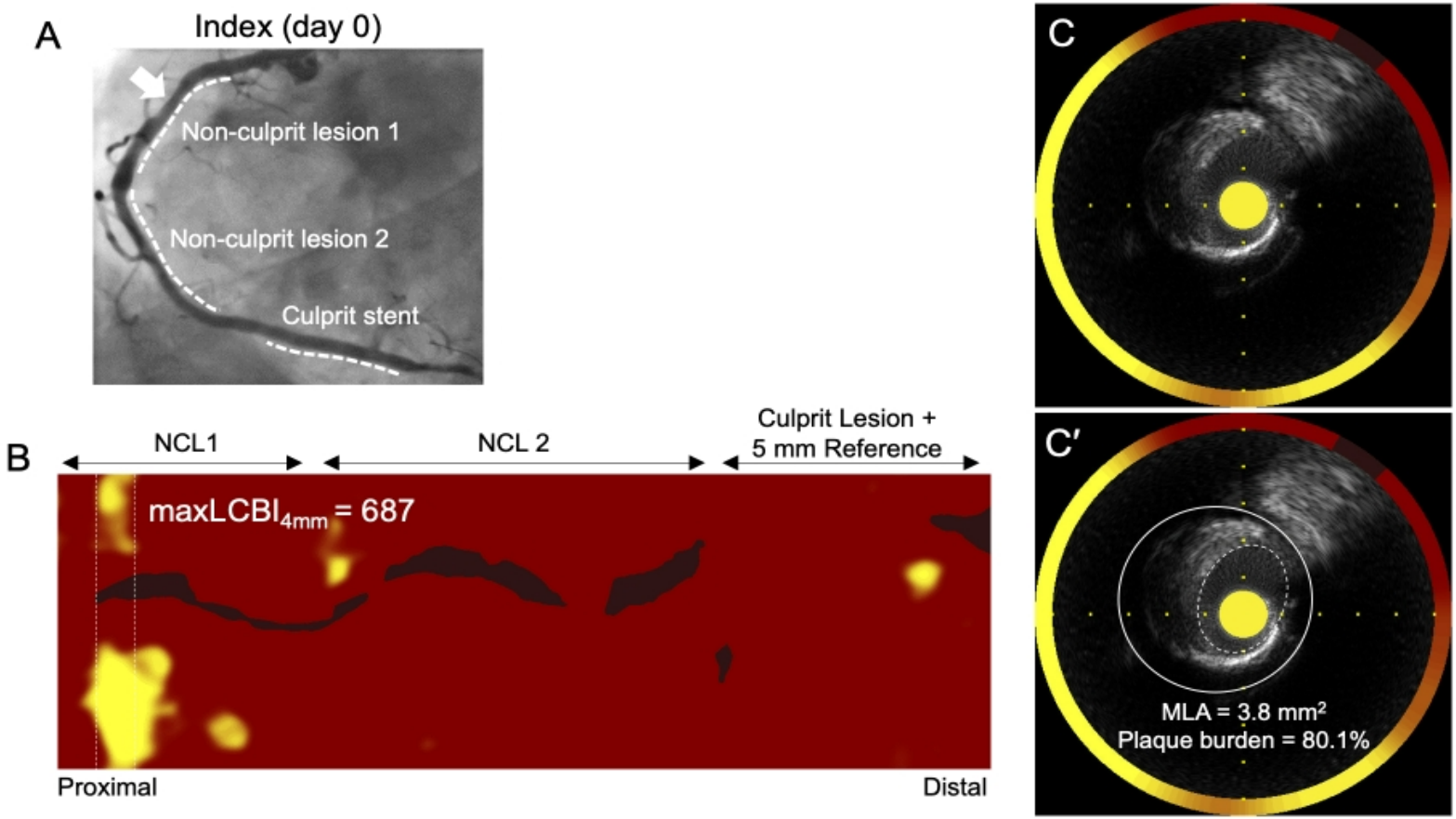
- **Angiography:** 1791 untreated lesions with diameter stenosis 30% were identified (median 2.0 [1.0, 3.0] per patient)
- **NIRS-IVUS:** Was performed in 2.7 0.6 coronary arteries per pt over a median total length 224 (182, 263) mm per patient
  - A total of 3629 untreated NCLs were prospectively identified by IVUS
    - Median 4.0 [3.0, 5.0] NCLs per patient
    - 24.3% of NCLs had a maxLCBI $_{4mm}$ ≥ the upper quartile of 324.7 (i.e. 32.5% lipid)
    - 21.7% of NCLs had plaque burden ≥70%
    - 37.9% of NCLs had MLA ≤4.0 mm ^{2}
- **One or more untreated NCLs:** With a maxLCBI $_{4mm}$ ≥324.7, plaque burden ≥70% or MLA ≤4.0 mm ^{2} were present in 58.8%, 59.0% and 75.6% of pts respectively

Imaging-related Adverse Events

- The primary safety outcome of intravascular imaging-related major complications requiring treatment occurred in 2/902 patients (0.2%)
  - 1 new stenosis due to spasm or dissection requiring balloon angioplasty
  - 1 acute occlusion, in retrospect due to air injection for which an additional stent was implanted

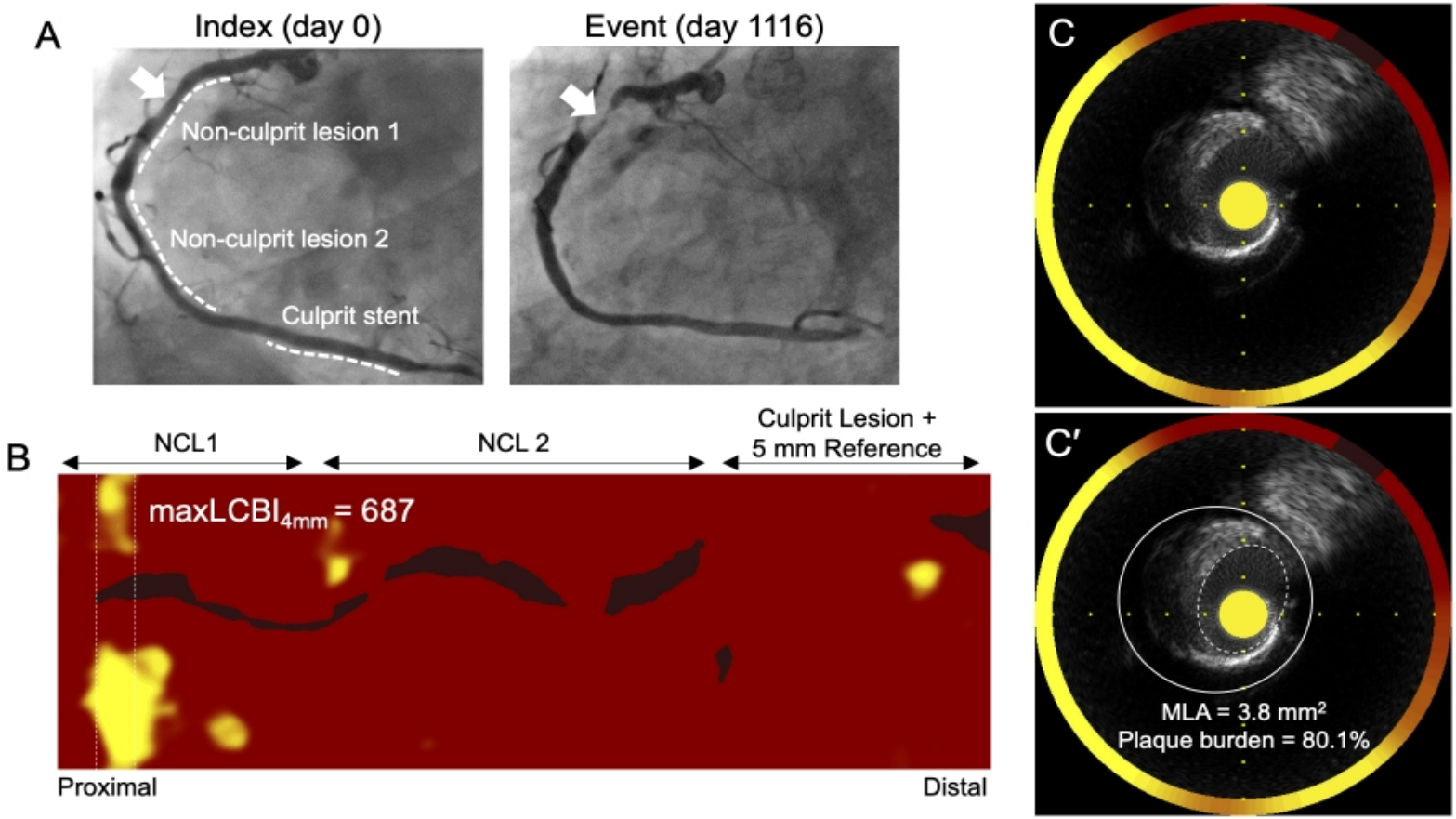
Representative case

An adverse event attributed to an untreated NCL



Representative case

An adverse event attributed to an untreated NCL



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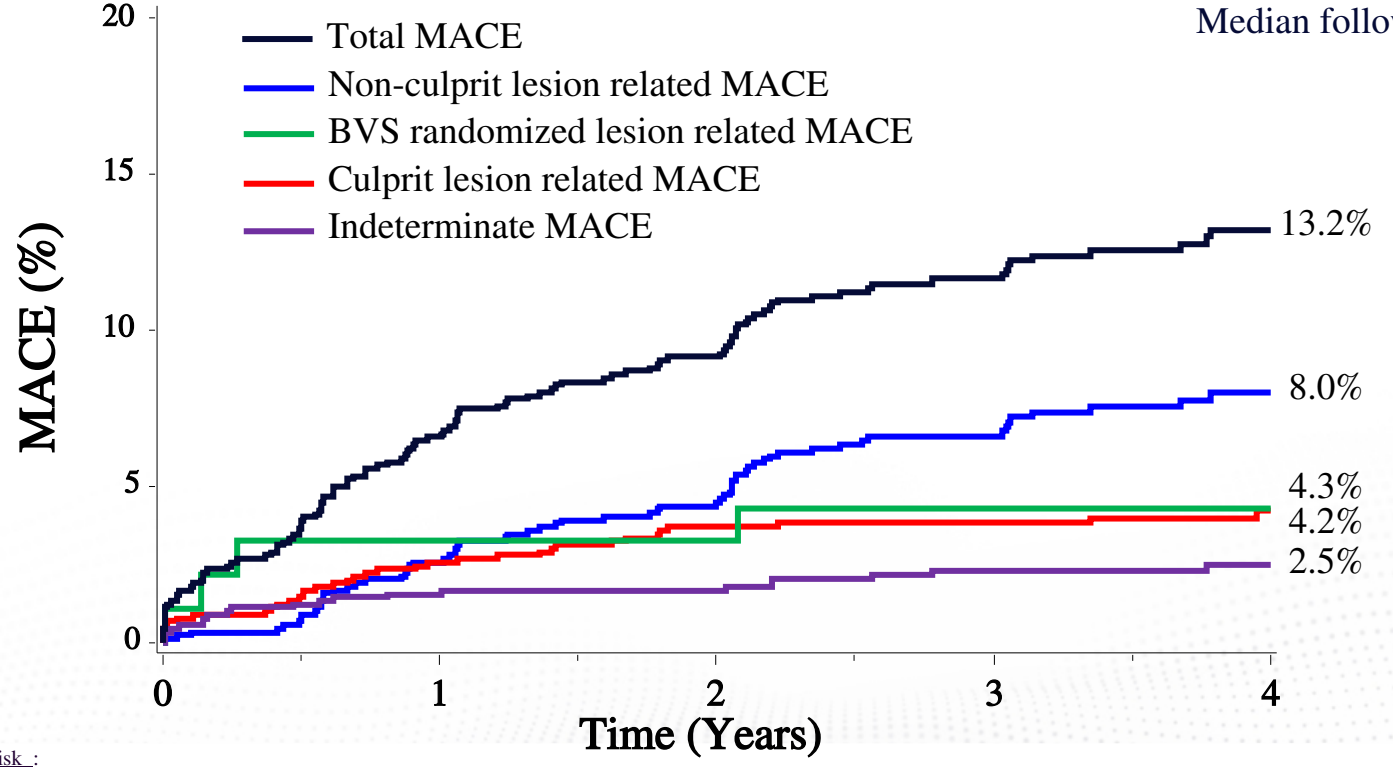
MACE Through 4-year Follow-up

Median follow-up 3.7 yrs



Number at risk :

Non-culprit	898	869	848	623	331
Culprit	898	869	855	646	351
BVS	93	90	90	78	45
Indeterminate	898	882	877	653	357
Total	898	837	810	593	317

MACE During the Entire Study Duration

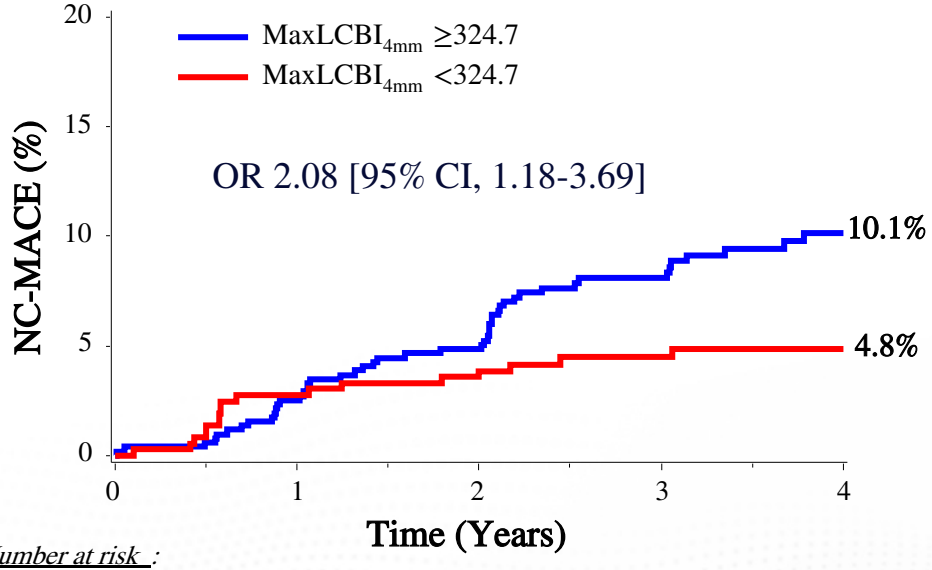
	All	Culprit lesion-related	Non-culprit lesion-related	BVS randomized lesion-related	Indeterminate
Major adverse cardiac events	14.4% (114)	4.6% (37)	8.0% (66)	4.3% (4)	3.3% (22)
- Cardiac death	1.6% (7)	0.0% (0)	0.0% (0)	0.0% (0)	1.6% (7)
- Myocardial infarction	6.9% (54)	2.7% (22)	3.2% (23)	2.2% (2)	1.6% (14)
- Procedure related	0.6% (5)	0.6% (5)	0.0% (0)	0.0% (0)	0.0% (0)
- Non-procedure related	6.3% (49)	2.2% (17)	3.2% (23)	2.2% (2)	1.6% (14)
- Unstable angina	1.3% (12)	0.2% (2)	1.0% (9)	1.1% (1)	0.0% (0)
- Progressive angina	5.7% (48)	1.8% (15)	4.5% (38)	1.1% (1)	0.1% (1)
- Requiring revascularization	4.2% (35)	1.5% (12)	3.1% (27)	1.1% (1)	0.1% (1)
- With rapid lesion progression	1.7% (14)	0.3% (3)	1.4% (12)	0.0% (0)	0.0% (0)

MACE Related to NCLs

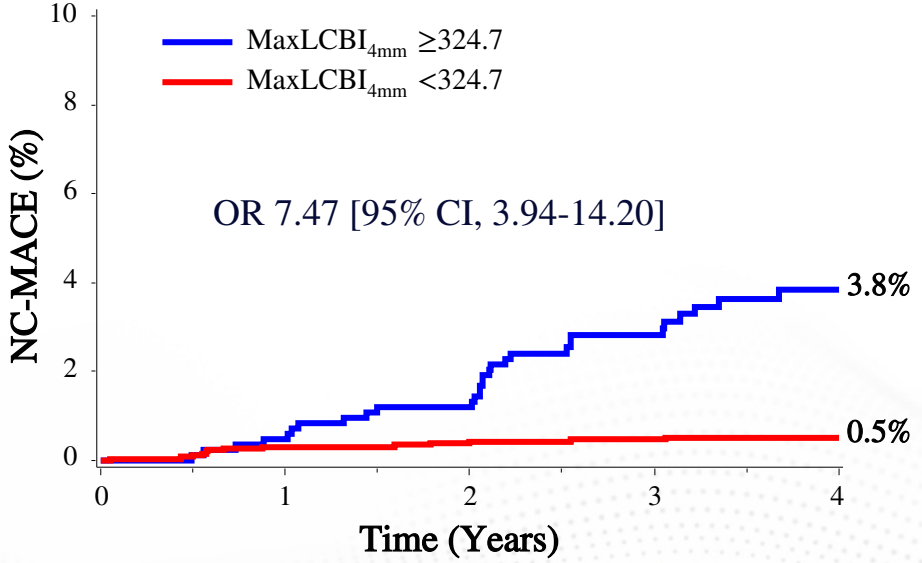
- There were 78 first NCL-MACE events
  - The mean QCA DS of these 78 NCLs was 46.9 ± 15.9% at baseline and 68.4 ± 17.7% at the time of the event
- Among these 78 NCLs, 44 (56.4%) were imaged at baseline by NIRS-IVUS
  - All had plaque burden of at least 56.2%
  - Median maxLCBI $_{4mm}$ was 473.9; 69.8% were ≥324.7

NCL-related MACE According to the Presence of HR Plaque Defined by Upper Quartile MaxLCBI $_{4mm}$

Patient-level events



Lesion-level events

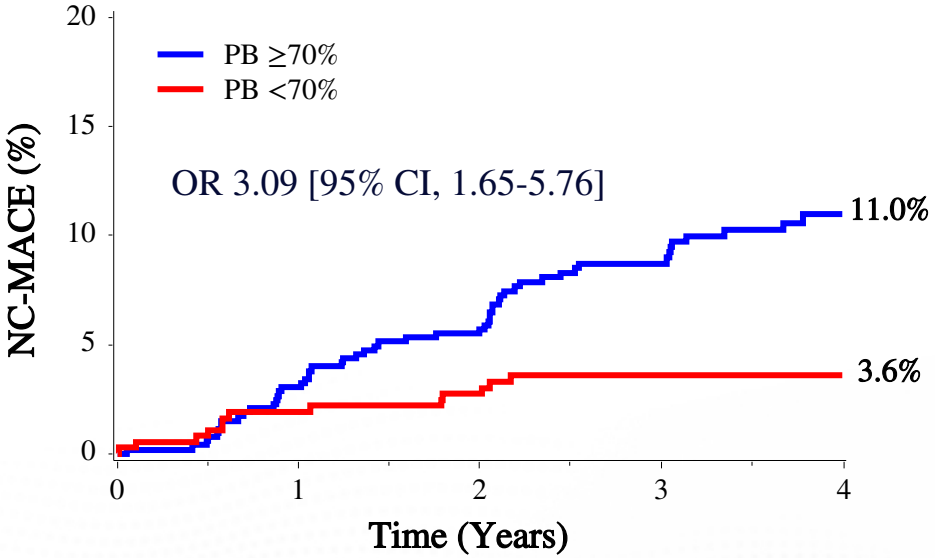


Number at risk :

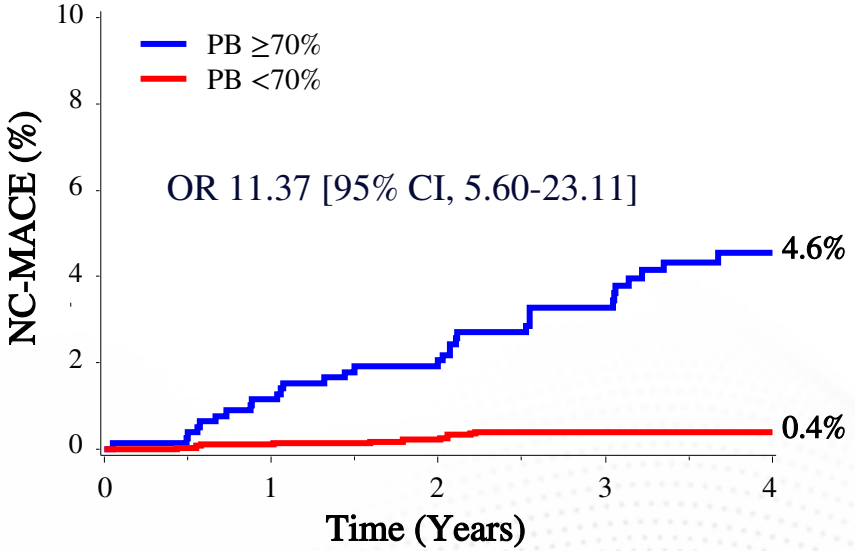
≥324.7	520	503	490	359	202	851	837	830	621	359
<324.7	364	352	345	255	127	2,649	2,623	2,610	1,976	1,092

NCL-related MACE According to the Presence of HR Plaque Defined by Plaque Burden ≥70%

Patient-level events



Lesion-level events



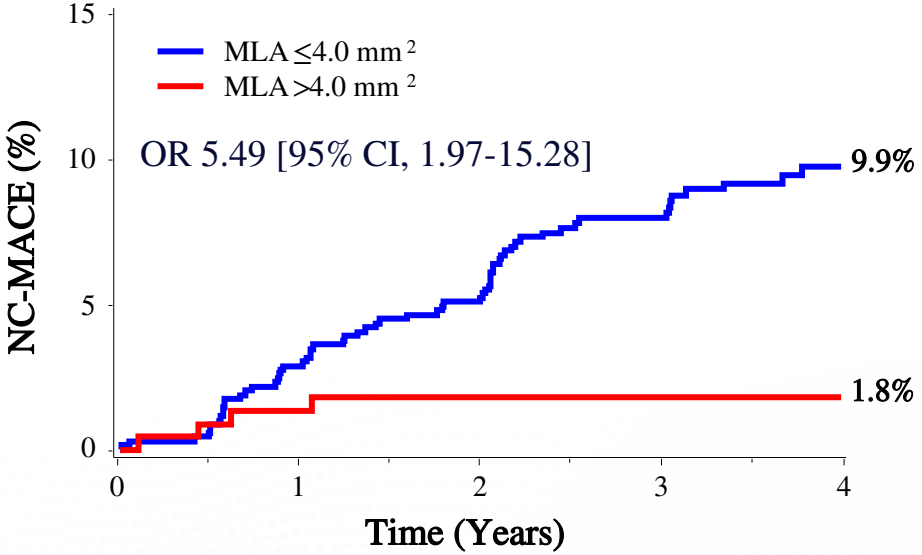
Number at risk :

PB ≥70%	530	510	494	367	199
PB <70%	368	359	354	256	132

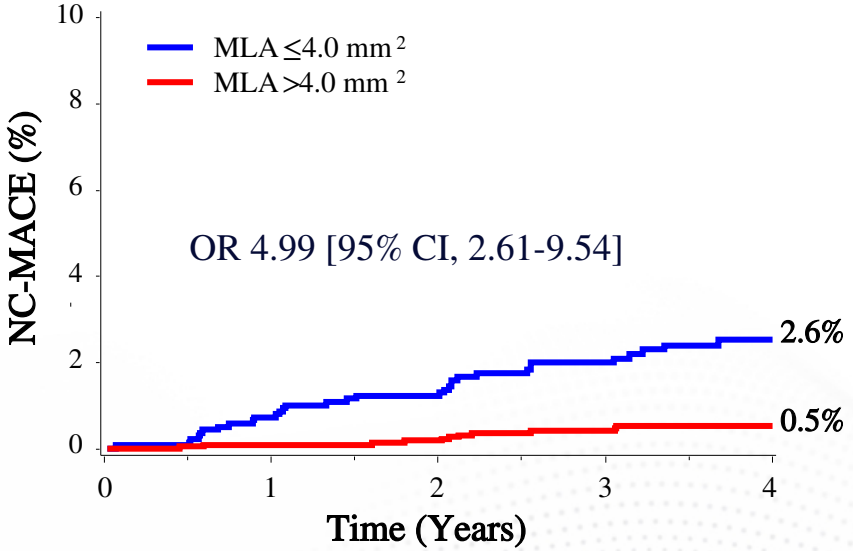
787	773	764	576	338
2,842	2,816	2,804	2,107	1,162

NCL-related MACE According to the Presence of HR Plaque Defined by MLA ≤4.0 mm ^{2}

Patient-level events



Lesion-level events



Number at risk :

≤4.0 mm ^{2}	679	654	636	465	259
>4.0 mm ^{2}	219	215	212	158	72

1,375	1,354	1,340	1,108	593
2,254	2,235	2,228	1,665	907

High-risk Plaque Characteristics and Patient-level NCL-MACE

High-risk plaque characteristic	Pts with ≥1 NCL with HRP characteristic	Pts without NCLs with HRP characteristic	OR (95% CI) Unadjusted
MaxLCBI$_{4mm}$ >324.7	N=520 patients	N=364 patients	
Non-culprit MACE	10.1% (48)	4.8% (17)	2.08 (1.18, 3.69)
- Myocardial infarction	4.4% (18)	1.1% (4)	3.20 (1.07, 9.55)
- Unstable angina	0.8% (4)	1.4% (5)	0.54 (0.14, 2.04)
- Progressive angina	6.1% (30)	2.3% (8)	2.73 (1.24, 6.03)
Plaque burden >70%	N=530 patients	N=368 patients	
Non-culprit MACE	11.0% (53)	3.6% (13)	3.09 (1.65, 5.76)
- Myocardial infarction	4.7% (20)	0.8% (3)	4.72 (1.39, 16.01)
- Unstable angina	1.0% (5)	1.1% (4)	0.85 (0.23, 3.17)
- Progressive angina	6.4% (32)	1.7% (6)	3.89 (1.61, 9.42)
MLA <4.0 mm^2	N=679 patients	N=219 patients	
Non-culprit MACE	9.9% (62)	1.8% (4)	5.49 (1.97, 15.28)
- Myocardial infarction	4.0% (22)	0.5% (1)	7.16 (0.96, 53.41)

Multivariable Models of NCL-related MACE

	OR (95% CI)	P-value
Patient-level models*		
Model 1: MaxLCBI $_{4mm}$ ≥324.7	2.27 (1.25-4.13)	0.007
Model 2: Plaque burden ≥70%	3.49 (1.83-6.63)	<0.001
Model 3: MLA ≤4.0 mm ^{2}	6.00 (2.12-17.00)	<0.001
Lesion-level models*		
Model 1: MaxLCBI $_{4mm}$ ≥324.7	7.83 (4.12-14.89)	<0.001
Model 2: Plaque burden ≥70%	12.94 (6.36-26.32)	<0.001
Model 3: MLA ≤4.0 mm ^{2}	4.97 (2.59-9.53)	<0.001

*Covariate adjusted for age, sex, prior PCI, HTN, diabetes, use of high-dose statin at discharge, total non-culprit segment length analyzed

Younger age and insulin-treated diabetes were also independent predictors of events

Multivariable Model of Lesion-level NCL-MACE with all 3 HR Plaque Characteristics

Lesion-level predictors*	OR (95% CI)
$MaxLCBI_{4mm}$ ≥324.7	3.80 (1.87-7.70)
Plaque burden ≥70%	5.37 (2.42-11.89)
Minimum lumen area ≤4.0 mm^2	1.85 (0.95-3.61)

*Covariate adjusted for age, sex, prior PCI, HTN, diabetes, use of high-dose statin at discharge, total non-culprit segment length analyzed

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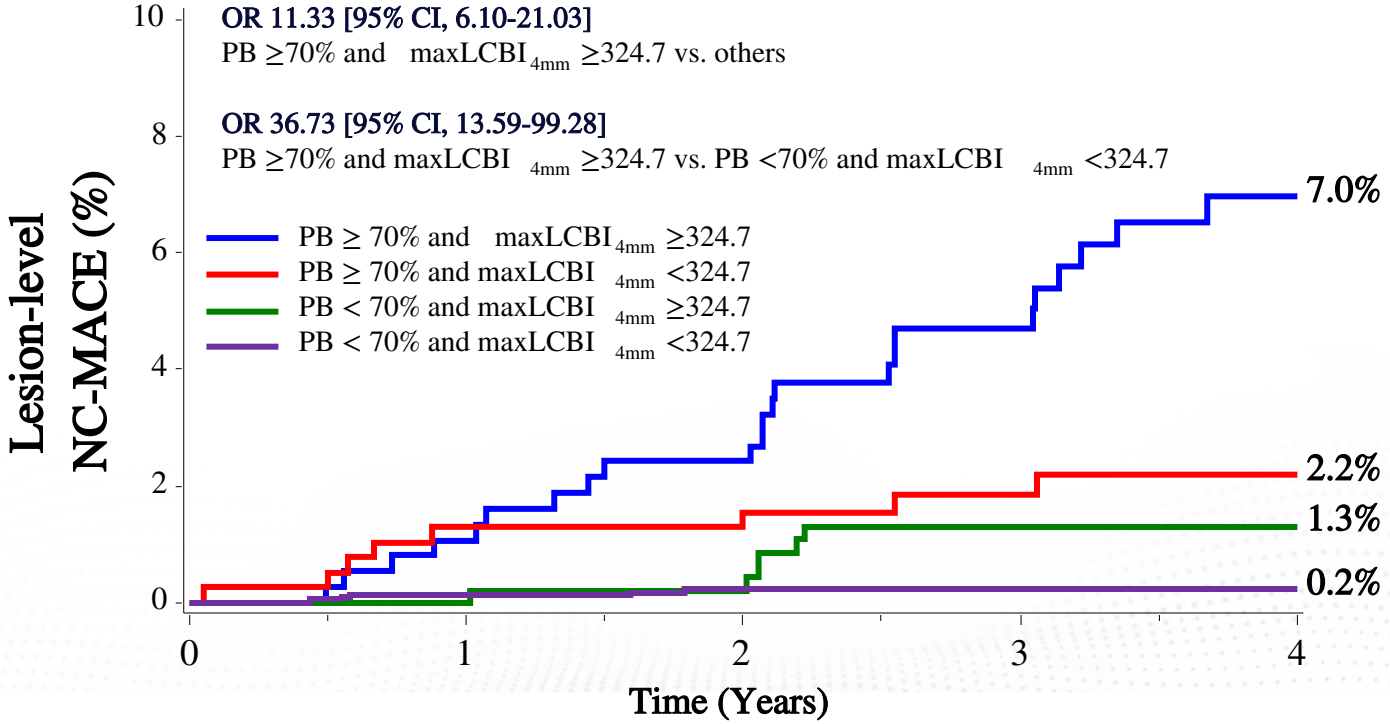
Lesion-level NCL-MACE According to the Presence of HR Plaque Defined by MaxLCBI $_{4mm}$ ≥324.7 and PB ≥70%



Number at risk :

PB ≥70% and maxLCBI $_{4mm}$ ≥324.7	374	368	362	271	162
PB ≥70% and maxLCBI $_{4mm}$ <324.7	391	383	381	293	168
PB <70% and maxLCBI $_{4mm}$ ≥324.7	477	469	468	350	197
PB <70% and maxLCBI $_{4mm}$ <324.7	2,258	2,240	2,229	1,683	924

Conclusions

- Following treatment of flow-limiting lesions in AMI with contemporary DES, MACE occurred in 14.4% of pts at median 3.7-year FU
  - 8.0% were caused by unanticipated events arising from untreated non-flow-limiting plaques vs. 4.6% from recurrent events at treated culprit lesions
- 3-vessel intracoronary imaging with NIRS-IVUS was safe
- NIRS identified lipid-rich angiographically mild non-flow-limiting plaques that were responsible for future coronary events
- The combination of lipid-rich plaque and large plaque burden identified vulnerable plaques that placed patients at especially high risk for future MACE
- Whether prophylactic treatment of these high-risk plaques is safe and effective was investigated in the integrated PROSPECT ABSORB trial

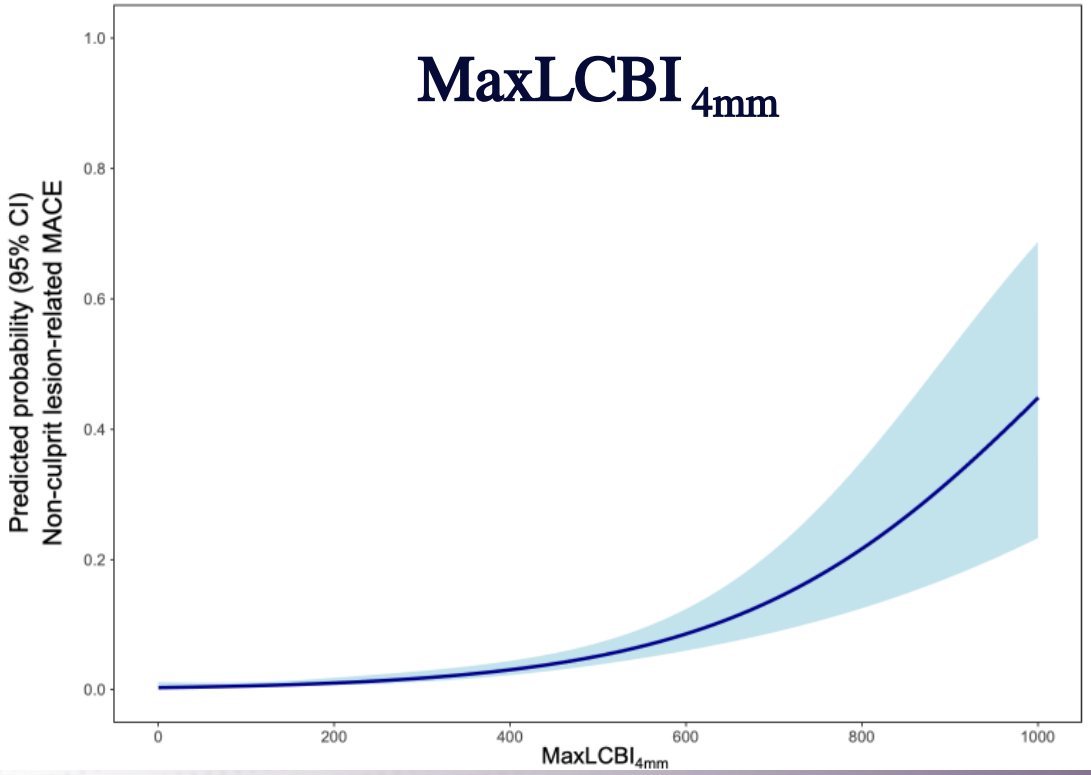
Back-up Slides

Power Analysis

- With 900 pts enrolled and 77 events, the study would have 88% power to detect the relationship between patients having one or more lesions with a specific high-risk plaque characteristic with an adjusted hazard ratio of 2.5 for patient-level adverse outcomes

- Anticipating 3,998 untreated non-culprit lesions, if 19% were high-risk the study would have 92% power to detect the relationship between high-risk plaque characteristics with an adjusted hazard ratio of 3.5 and lesion-level adverse outcomes

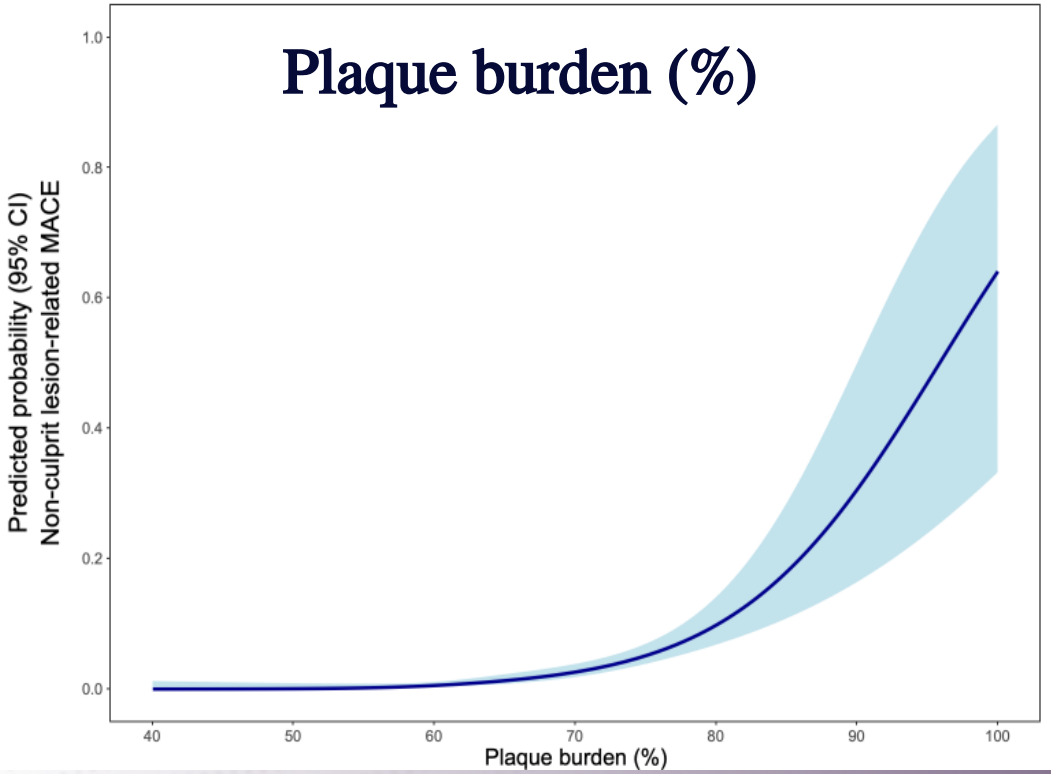
Spline and ROC Analyses of the Continuous Relationship Between HR Plaque Characteristics and Lesion-level NCL-MACE



ROC analysis

AUC (95% CI)	0.79 (0.72, 0.86)
Optimal cutoff (95% CI)	324.6 (129.7, 473.6)
Sensitivity	0.70
Specificity	0.76
Accuracy	0.76

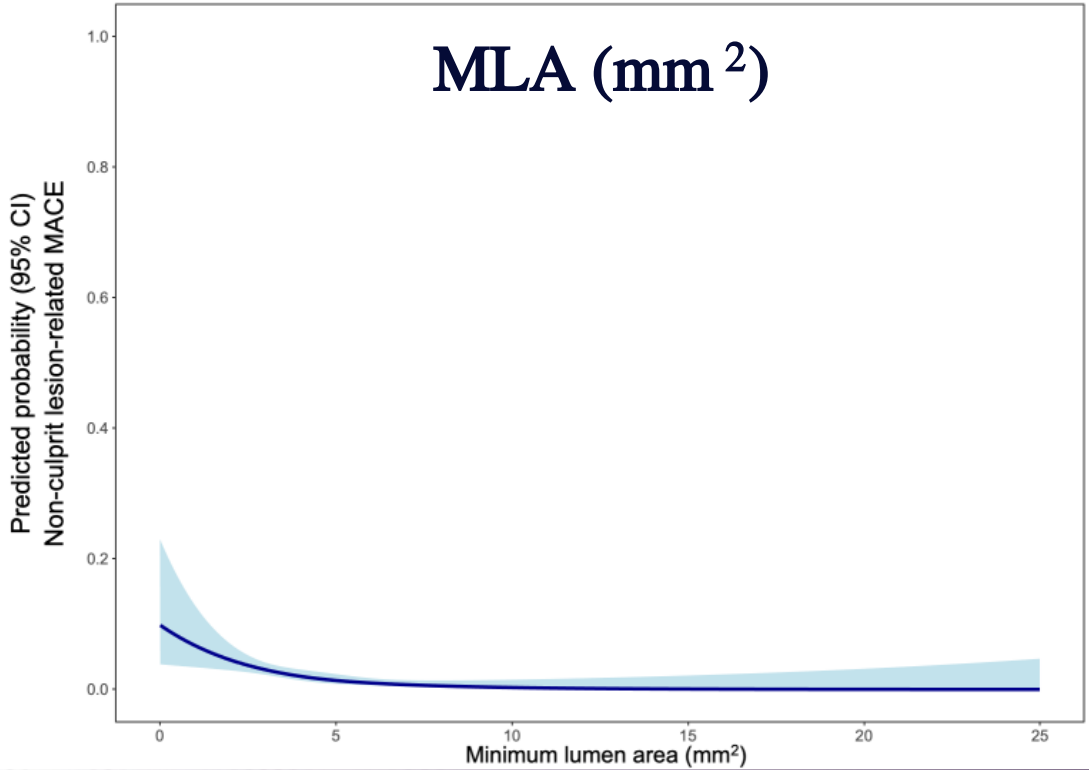
Spline and ROC Analyses of the Continuous Relationship Between HR Plaque Characteristics and Lesion-level NCL-MACE



ROC analysis

AUC (95% CI)	0.84 (0.79, 0.89)
Optimal cutoff (95% CI)	69.8% (66.7, 70.7)
Sensitivity	0.82
Specificity	0.78
Accuracy	0.79

Spline and ROC Analyses of the Continuous Relationship Between HR Plaque Characteristics and Lesion-level NCL-MACE



ROC analysis

AUC (95% CI)	0.72 (0.65, 0.78)
Optimal cutoff (95% CI)	4.25 mm 2 (3.15, 5.22)
Sensitivity	0.80
Specificity	0.59
Accuracy	0.59

Selected Medication Use

Medication	Discharge	1 year	2 years
Aspirin or a P2Y12 inhibitor	99.9% (897/898)	95.6% (843/882)	93.6% (820/876)
- Aspirin	97.3% (874/898)	92.9% (819/882)	90.3% (791/876)
- P2Y12 inhibitor	99.4% (893/898)	36.1% (319/883)	7.6% (67/876)
- Clopidogrel or ticlopidine	8.7% (78/898)	8.0% (71/883)	4.1% (36/876)
- Clopidogrel	8.7% (78/898)	7.8% (69/883)	4.1% (36/876)
- Ticlopidine	0% (0/898)	0.2% (2/883)	0% (0/876)
- Prasugrel or ticagrelor	90.8% (815/898)	28.1% (248/883)	3.5% (31/876)
- Prasugrel	0.9% (8/898)	1.0% (9/883)	0.2% (2/876)
- Ticagrelor	89.9% (807/898)	27.1% (239/883)	3.3% (29/876)
DAPT	96.9% (870/898)	33.4% (295/882)	4.3% (38/875)
Oral anticoagulant (VKA or DOAC)	5.7% (51/897)	7.1% (63/883)	7.9% (69/876)
ACEi, ARB or ARNI	54.6% (490/898)	59.1% (522/883)	59.4% (520/875)
Beta-blocker	75.3% (676/898)	72.2% (637/882)	67.7% (592/875)
Statin	98.8% (887/898)	95.2% (841/883)	93.5% (819/876)
- High-dose statin*	91.6% (823/898)	84.3% (744/883)	81.6% (715/876)
Ezetimibe	1.6% (14/898)	9.3% (82/883)	11.6% (102/876)
PCSK9 inhibitor	0.2% (2/898)	0.1% (1/882)	0.2% (2/874)
Other lipid-lowering agents	0.0% (0/898)	0.2% (2/882)	0.2% (2/874)

*Atorvastatin ≥40 mg/day or rosuvastatin ≥20 mg/day.

Baseline Imaging of NCLs: Angiography

Patient-level data	N=898
Number of angiographic NCLs*	2.0 (1.0, 3.0)
Number of diseased vessels (with ≥1 angiographic NCL)	1.0 (1.0, 2.0)
- Zero	18.6% (167/898)
- One	36.5% (328/898)
- Two	32.3% (290/898)
- Three	12.6% (113/898)
Lesion-level data*	**N=1791 †**
Vessel location of angiographic non-culprit lesions	
- Left anterior descending coronary artery	36.2% (649/1791)
- Left circumflex coronary artery	29.6% (530/1791)
- Right coronary artery	33.7% (603/1791)
- Left main coronary artery	0.5% (9/1791)
Lesion length (mm)	9.3 (6.3, 14.5)
Reference vessel diameter (mm)	2.56 (2.11, 3.12)
Minimum lumen diameter (mm)	1.43 (1.02, 1.82)
Diameter stenosis (%)	43.0 (36.5, 54.6)
Thrombus, ulceration, intimal flap, or aneurysm	1.2% (21/1791)
Calcification	3.7% (67/1789)

*Lesions with angiographic diameter stenosis ≥30%. †Excludes 82 angiographic and 94 NIRS-IVUS randomized NCLs.

Baseline Imaging of NCLs: IVUS I

Patient-level data	N=898
Total coronary artery length imaged (mm)	224.3 (181.9, 263.1)
Total length of non-culprit segments analyzed (mm)	154.2 (116.0, 194.6)
Number of vessels imaged	3.0 (2.0, 3.0)
Number of IVUS NCLs*	4.0 (3.0, 5.0)
Number of diseased vessels (with ≥1 IVUS NCL)	2.0 (2.0, 3.0)
- Zero	1.7% (15/898)
- One	12.7% (114/898)
- Two	36.2% (325/898)
- Three	49.4% (444/898)
Patients with any NCLs with plaque burden ≥70%	59.0% (530/898)
Patients with any NCLs with MLA ≤4.0 mm^2	75.6% (679/898)
Patients with any NCLs with plaque rupture	15.0% (135/898)
Lesion-level data*	**N=3629†**
Vessel location of IVUS non-culprit lesions	
- Left anterior descending coronary artery	35.9% (1302/3629)
- Left circumflex coronary artery	27.2% (988/3629)
- Right coronary coronary artery	34.7% (1258/3629)
- Left main coronary artery	2.2% (81/3629)
NCL in originally-treated culprit vessel	41.3% (1500/3629)

*Untreated coronary segments ≥2 mm in length with ≥40% plaque burden. †Excludes 82 angiographic and 94 NIRS-IVUS randomized NCLs.

Baseline Imaging of NCLs: IVUS II

Lesion-level data	N=3629
Maximum plaque burden (%)	61.0 (53.6, 68.7)
- Maximum plaque burden ≥70%	21.7% (787/3629)
Percent plaque volume (%)	49.8 (46.1, 54.4)
Disease arc at maximum plaque burden site (°)	180 (110, 290)
- Concentric plaque (disease arc ≥330°)	21.3% (772/3629)
MLA (mm^2)	4.8 (3.2, 7.1)
- MLA ≤4.0 mm^2	37.9% (1375/3629)
Vessel area at MLA (mm^2)	12.6 (8.9, 17.0)
Remodeling index (RI)	0.90 (0.77, 0.98)
- Positive remodeling (RI >1.0)	17.4% (632/3629)
- Intermediate remodeling (RI 0.88-1.00)	37.8% (1373/3629)
- Negative remodeling (RI <0.88)	44.8% (1624/3629)
Distance from ostium to MLA site (mm)	30.4 (13.2, 53.5)
Lesion length (mm)	12.0 (6.0, 24.0)
Plaque rupture	4.2% (152/3629)
Superficial attenuated plaque	19.0% (690/3629)
- Maximum arc of superficial attenuated plaque (°)	76 (61, 96)
Superficial calcified plaque	55.6% (2019/3629)
- Calcified nodule	3.3% (121/3629)

Baseline Imaging of NCLs: NIRS

Patient-level data	N=884
$MaxLCBI_{4mm}$	366.1 (247.2, 476.1)
$MaxLCBI_{4mm}$ ≥324.7	58.8% (520/884)
$MaxLCBI_{4mm}$ ≥400	42.8% (378/884)
Lesion-level data	**N=3500†**
$MaxLCBI_{4mm}$	166.8 (17.5, 320.4)
$MaxLCBI_{4mm}$ ≥324.7	24.3% (851/3500)
$MaxLCBI_{4mm}$ ≥400	15.1% (530/3500)
Maximum LRP burden (%)	16.2 (6.4, 28.9)
Percent LRP volume (%)	3.4 (0.3, 9.6)

†Excludes 82 angiographic and 94 NIRS-IVUS randomized NCLs.

Baseline Imaging of NCLs: NIRS-IVUS

Patient-level data	N=884
Patients with NCLs with 0 high-risk plaque characteristics ††	12.2% (108/884)
Patients with NCLs with 1 of 3 high-risk plaque characteristics	87.8% (776/884)
Patients with NCLs with 2 of 3 high-risk plaque characteristics	67.6% (598/884)
Patients with NCLs with 3 of 3 high risk-plaque characteristics	38.7% (342/884)
Lesion-level data*	**N=3500†**
Lesions with 0 high-risk plaque characteristics ††	46.4% (1624/3500)
Lesions with 1 of 3 high-risk plaque characteristics	53.6% (1876/3500)
- With angiographic diameter stenosis ≥30%	32.5% (609/1876)
Lesions with 2 of 3 high-risk plaque characteristics	22.8% (799/3500)
- With angiographic diameter stenosis ≥30%	47.6% (380/799)
Lesions with 3 of 3 high-risk plaque characteristics	8.3% (290/3500)
- With angiographic diameter stenosis ≥30%	53.1% (154/290)
Plaque phenotype	
- LRP (lesion max maxLCBI $_{4mm}$ ≥324.7) with superficial attenuated plaque	10.3% (360/3500)
- LRP without superficial attenuated plaque	20.4% (714/3500)
- Superficial calcified LRP	4.0% (140/3500)
- No LRP	54.9% (1922/3500)

*Lesions with angiographic diameter stenosis ≥30%. †Excludes 82 angiographic and 94 NIRS-IVUS randomized NCLs.

††Pre-specified high-risk plaque characteristics include maxLCBI4mm ≥324.7, maximum plaque burden ≥70%, and MLA ≤4.0 mm [2].

Events During the Entire Study Duration

	All	Culprit lesion-related	Non-culprit lesion-related	BVS randomized lesion-related	Indeterminate
All-cause death	3.8% (18)	0.0% (0)	0.0% (0)	0.0% (0)	3.8% (18)
- Cardiovascular death	1.7% (8)	0.0% (0)	0.0% (0)	0.0% (0)	1.7% (8)
- CV, non-cardiac death	0.1% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.1% (1)
- Non-cardiovascular death	2.1% (10)	0.0% (0)	0.0% (0)	0.0% (0)	2.1% (10)
Symptom-driven revascularization	9.4% (78)	3.7% (31)	6.5% (54)	4.3% (4)	0.1% (1)
- PCI	8.5% (71)	3.4% (28)	5.8% (48)	4.3% (4)	0.0% (0)
- CABG surgery	0.9% (8)	0.3% (3)	0.7% (6)	0.0% (0)	0.1% (1)
Stent thrombosis, def/prob	0.8% (7)	0.6% (5)	0.0% (0)	1.1% (1)	0.1% (1)
- Definite	0.7% (6)	0.6% (5)	0.0% (0)	1.1% (1)	0.0% (0)
- Probable	0.1% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.1% (1)

Limitations

- The NCL-MACE rate was somewhat lower than expected.
  - ¡ Nonetheless, sufficient events accrued during FU to demonstrate strong relationships between the 3 pre-specified HRP characteristics and MACE
- Most NCL events were non-procedural MIs and progressive angina requiring treatment
  - ¡ Absent FU angiography all cardiac deaths and some MIs were classified as indeterminate
- The present results were derived from use of a specific combination NIRS-IVUS imaging catheter
  - ¡ Whether OCT or other instruments would be as predictive or provide incremental prognostic utility is uncertain