PLACE 2026

PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

CONGRESSO

ROMA, 25 - 27 Giugno 2026

Session: “How should I treat?”: Placca Vulnerabile

Background & esperienze cliniche

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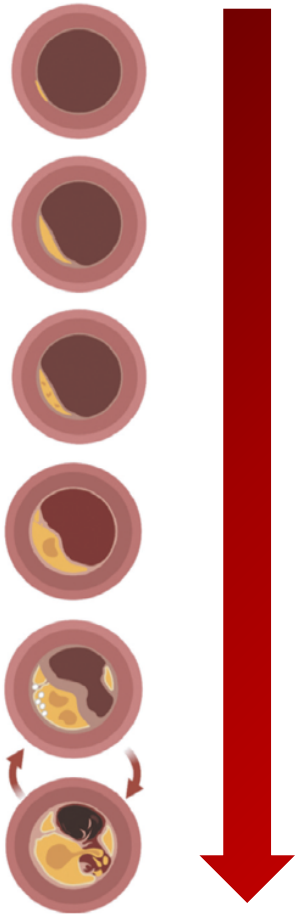
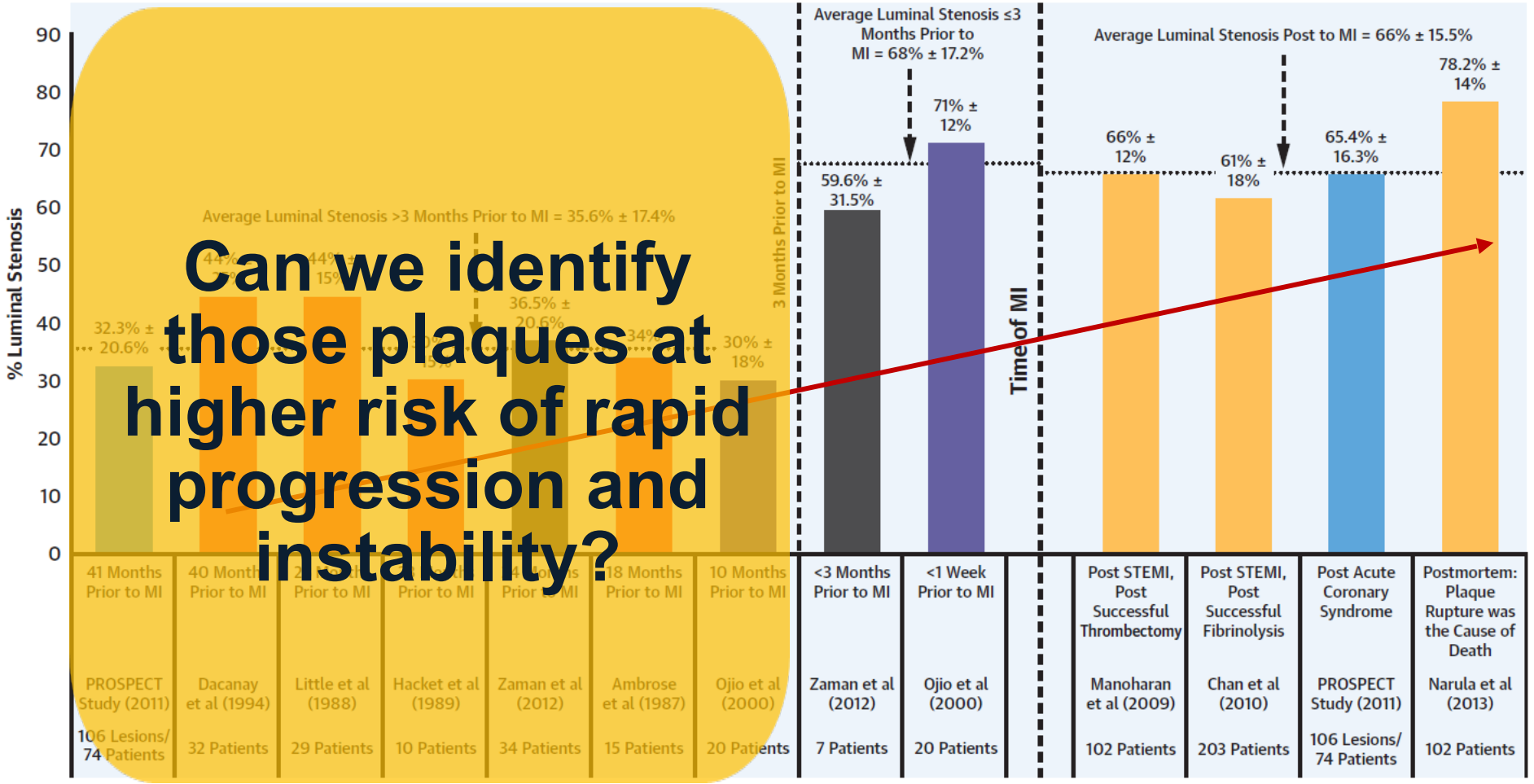
Treatment of high-risk plaques

Rationale for identifying and treating HRPs

Plaque progression before the occurrence of the acute coronary event



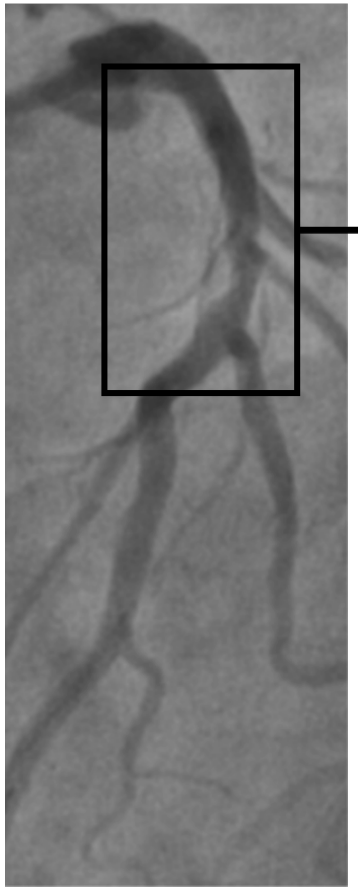


Can we identify those plaques at higher risk of rapid progression and instability?

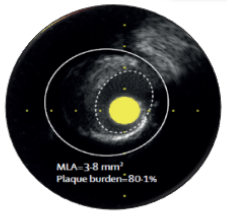
Treatment of high-risk plaques

Rationale for identifying and treating HRPs

Lesion-level prognostic meaning of nonobstructive high-risk plaques

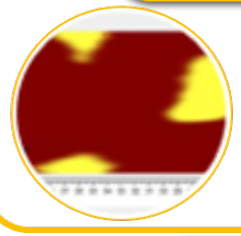


IVUS



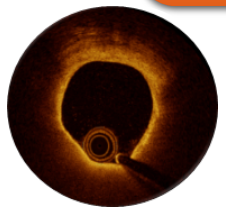
Large plaque burden

IVUS-NIRS



Lipid-rich plaques

OCT



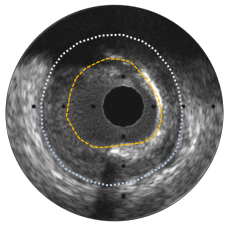
Thin cap fibroatheroma

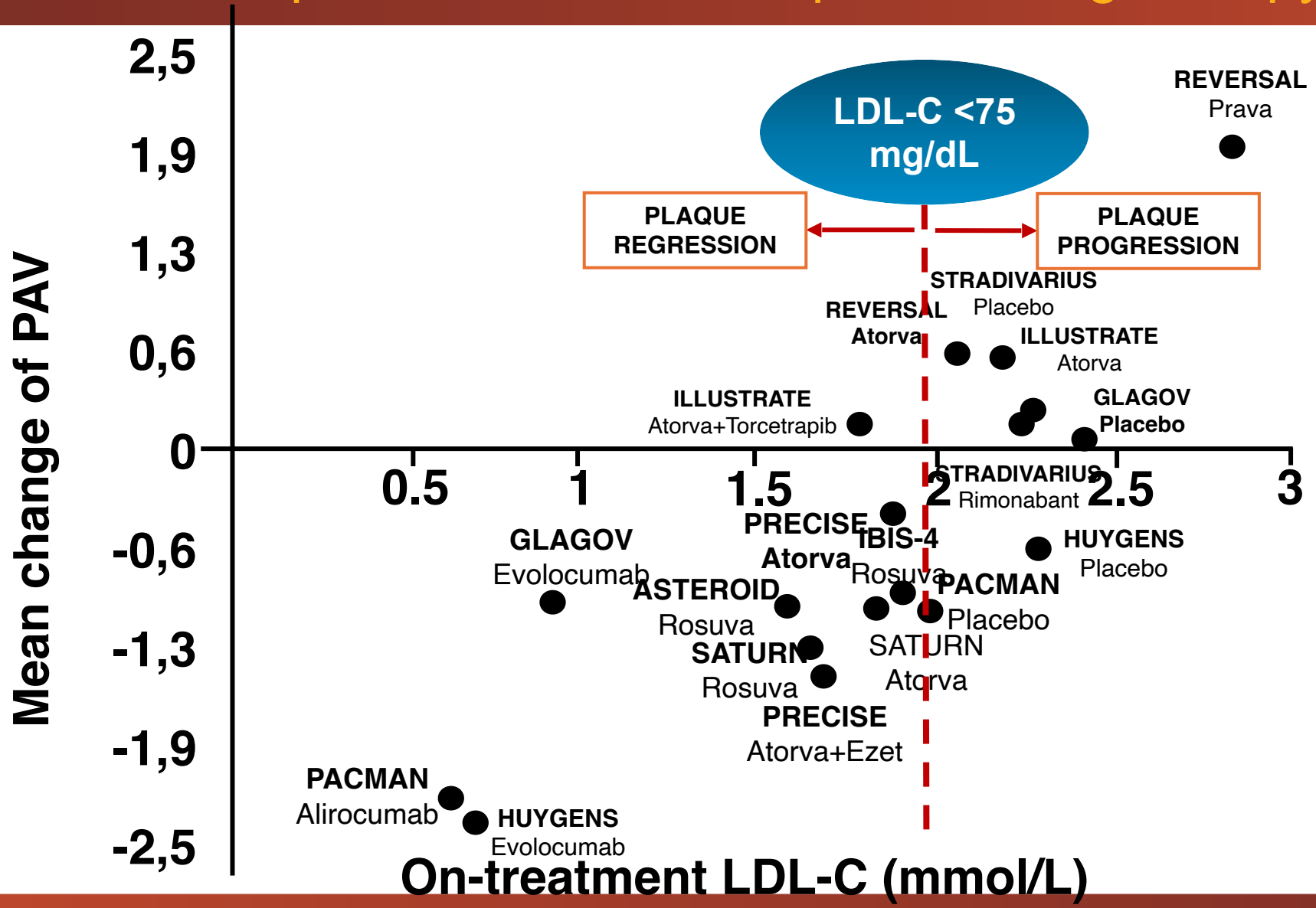
Risk of lesions-level MI

4-y	PROSPECT II	*Lancet 2021*	HR 4.72 (1.39-16.01)
4-y	PROSPECT II	*Lancet 2021*	HR 3.20 (1.07-9.55)
4-y	Jiang et al	*JACC 2023*	HR 3.10 (0.83-11.58)
5-y	COMBINE	*EuroIntv 2023*	HR 9.41 (2.01-44.1)
5-y	CLIMA	*JACC Intv 2025*	HR 7.02 (2.37-20.77)
5-y	Pectus&COMBINE	*Circ Intv 2025*	HR 9.41 (2.01-44.07)
6-y	Kubo et al.	*EHJ-CI 2021*	HR 10.41 (6.48–16.73)

Treatment of high-risk plaques

What we can expect from intensive lipid-lowering therapy





Treatment of high-risk plaques

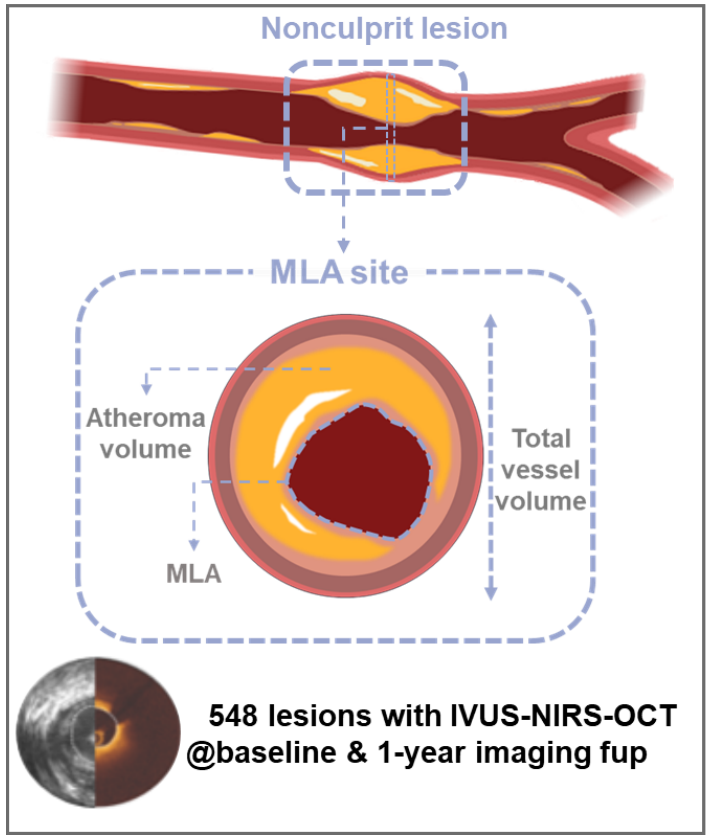
What we can expect from intensive lipid-lowering therapy

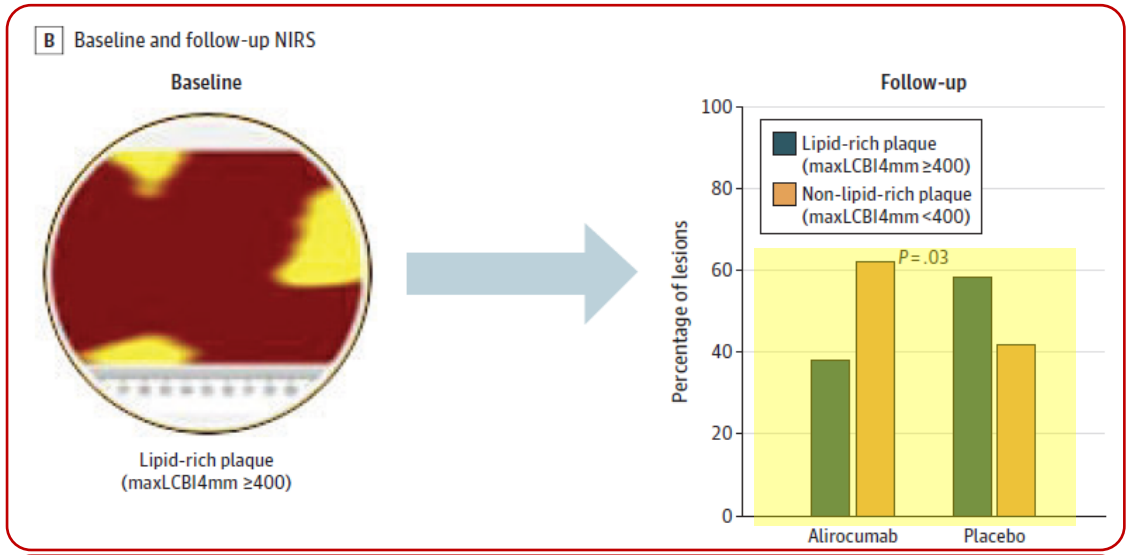
Effects of PCSK9i on HRPs

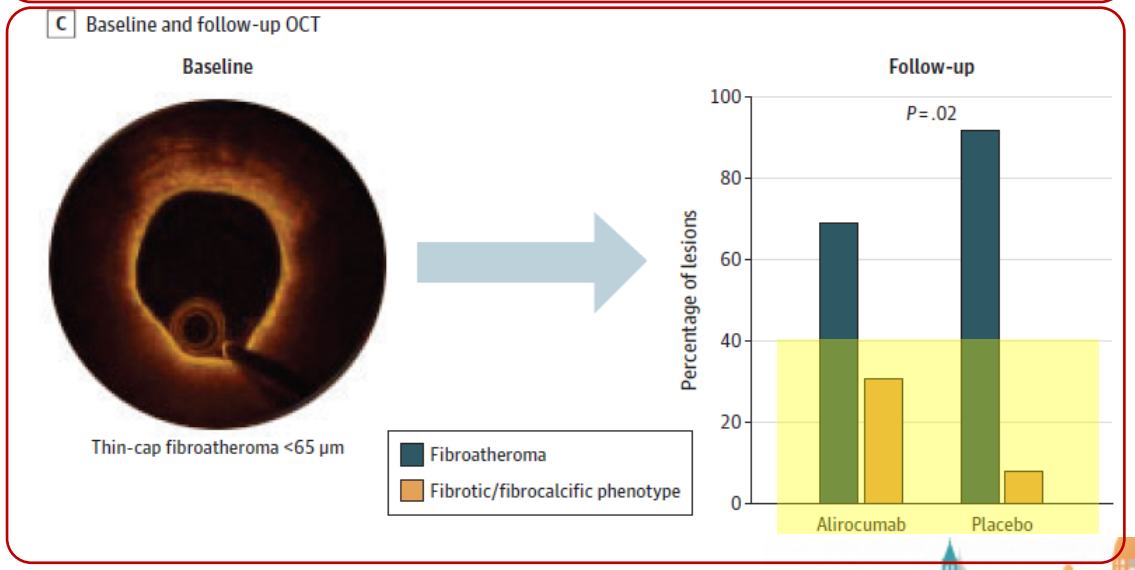
The PACMAN-AMI lesion-level analysis

265 patients with AMI randomised to PCSK9i or high-intensity statin alone

52 weeks IVUS-NIRS and OCT follow-up

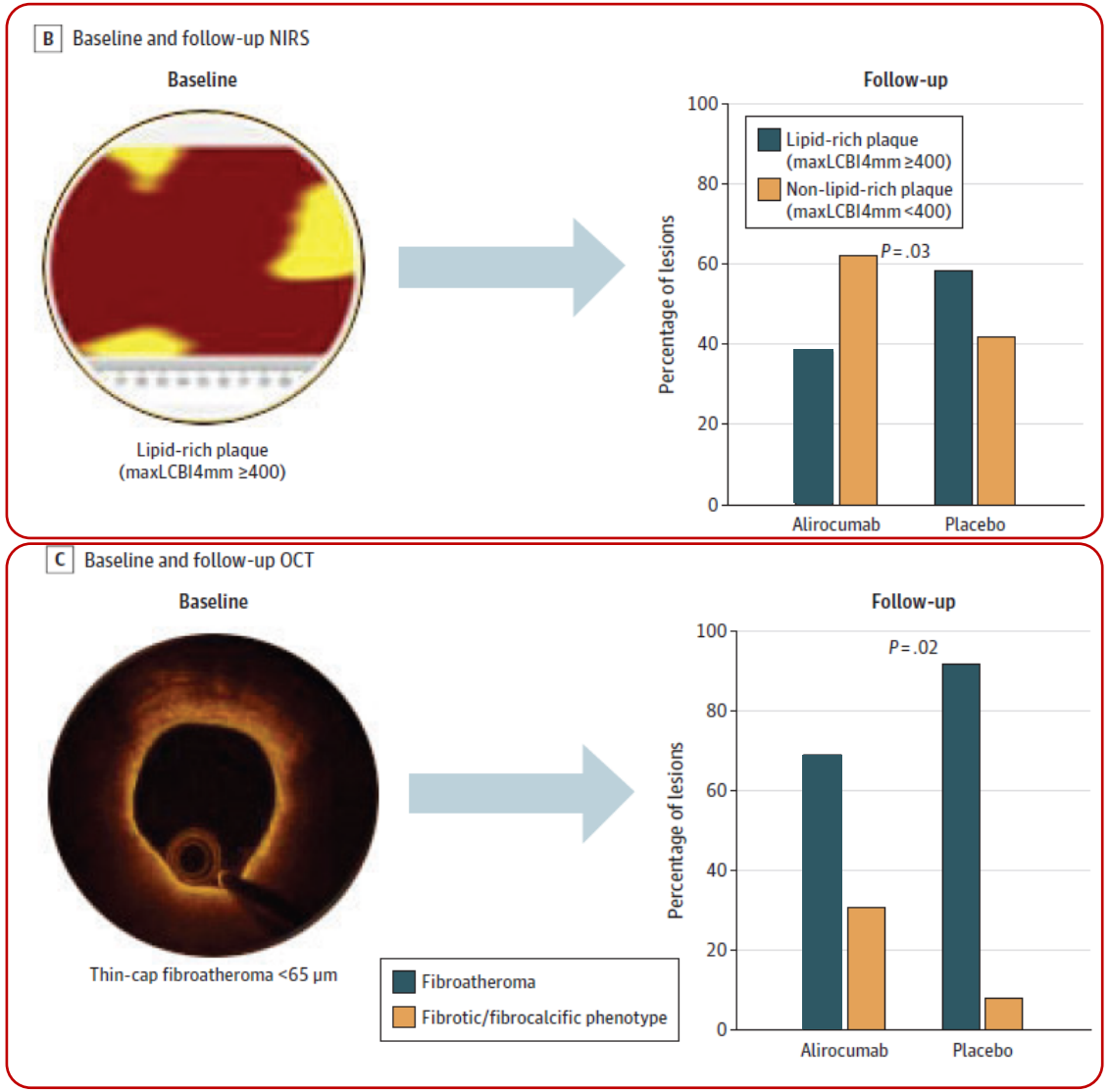






Treatment of high-risk plaques

Intensive LLT may not be sufficient in selected high-risk pts/lesions



Despite 20 mg/dL of LDL, at 1-y fup:

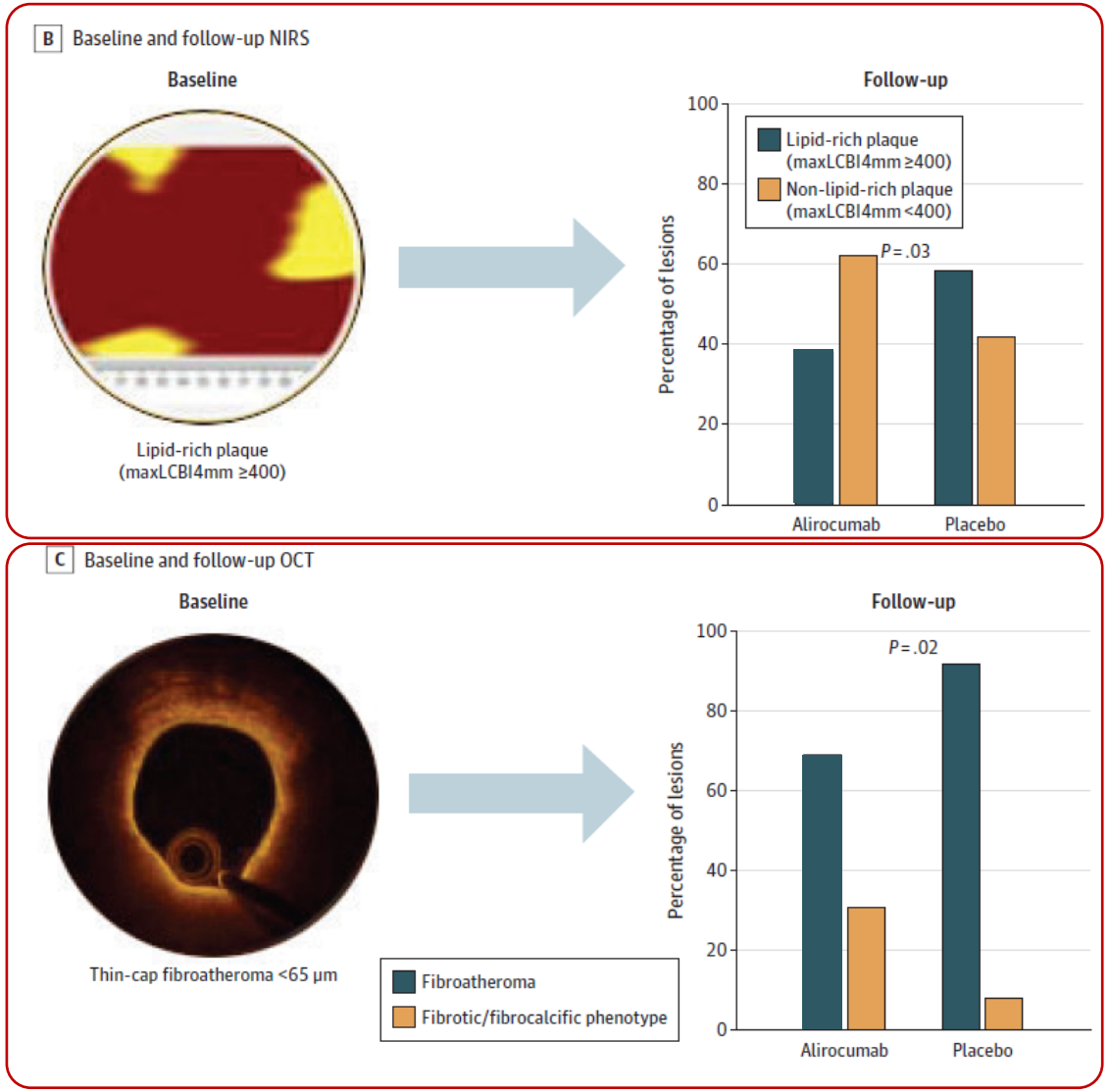
- **40% of LRPs were still lipid-rich**
- **65% of plaques did not stabilise into fibrocalcific plaques**

Residual coronary risk

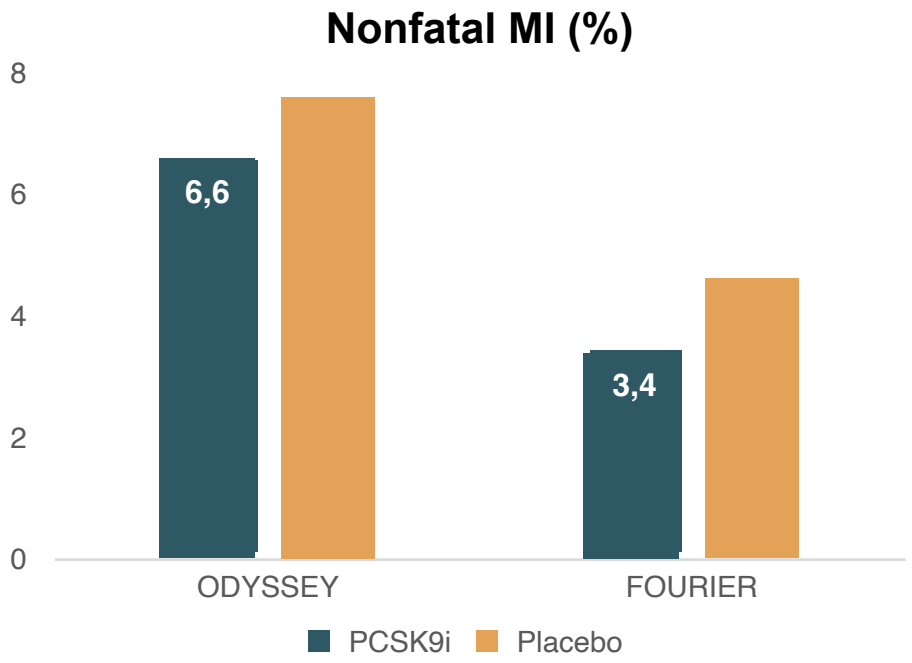
Biccirè et al JAMA Cardiol. 2024;9:1082-1092.

Treatment of high-risk plaques

Why OMT may not be sufficient in selected high-risk lesions/patients



Reduction in MIs with PCSK9i



Alirocumab and Cardiovascular Outcomes after Acute Coronary Syndrome

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Biccirè et al JAMA Cardiol. 2024;9:1082-1092.

Treatment of high-risk plaques

Intensive LLT may not be sufficient in selected high-risk pts/lesions

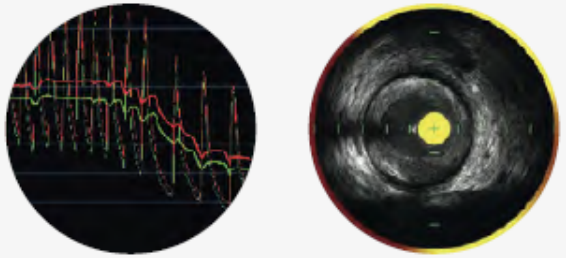
The FITTER trial

Short-term effects of PCSK9i on functionally significant HRPs of AMI pts

A Population

ACS patients undergoing PCI of the culprit lesion with an important non-culprit lesion (FFR 0.67-0.85)

B Non-culprit lesion measurements



FFR IVUS-NIRS

C Intervention

150 patients included and randomised

74 Evolocumab + High-dose statin

76 Placebo + High-dose statin

Repeat FFR and IVUS-NIRS after 12 weeks

D Results

FFR

	Evolocumab	Placebo
Baseline	0.78	0.78
Follow-up	0.77	0.79
Adjusted mean change (95% CI)	0.00 (–0.02 to 0.02)	0.01 (–0.01 to 0.03)

Difference compared to placebo:
–0.01 (95% CI: –0.03 to 0.01; p=0.6)
Overall change: 0.00 (95% CI: –0.01 to 0.01)

$maxLCBI_{4mm}$

	Evolocumab	Placebo
Baseline	357.4	359.9
Follow-up	324.2	318.0
Adjusted mean change (95% CI)	–27.8 (–72.2 to 16.6)	–35.6 (–82.5 to 11.4)

Difference compared to placebo:
7.8 (95% CI: –40.9 to 56.4; p=0.8)
Overall change: –37.3 (95% CI: –63.2 to –11.3)

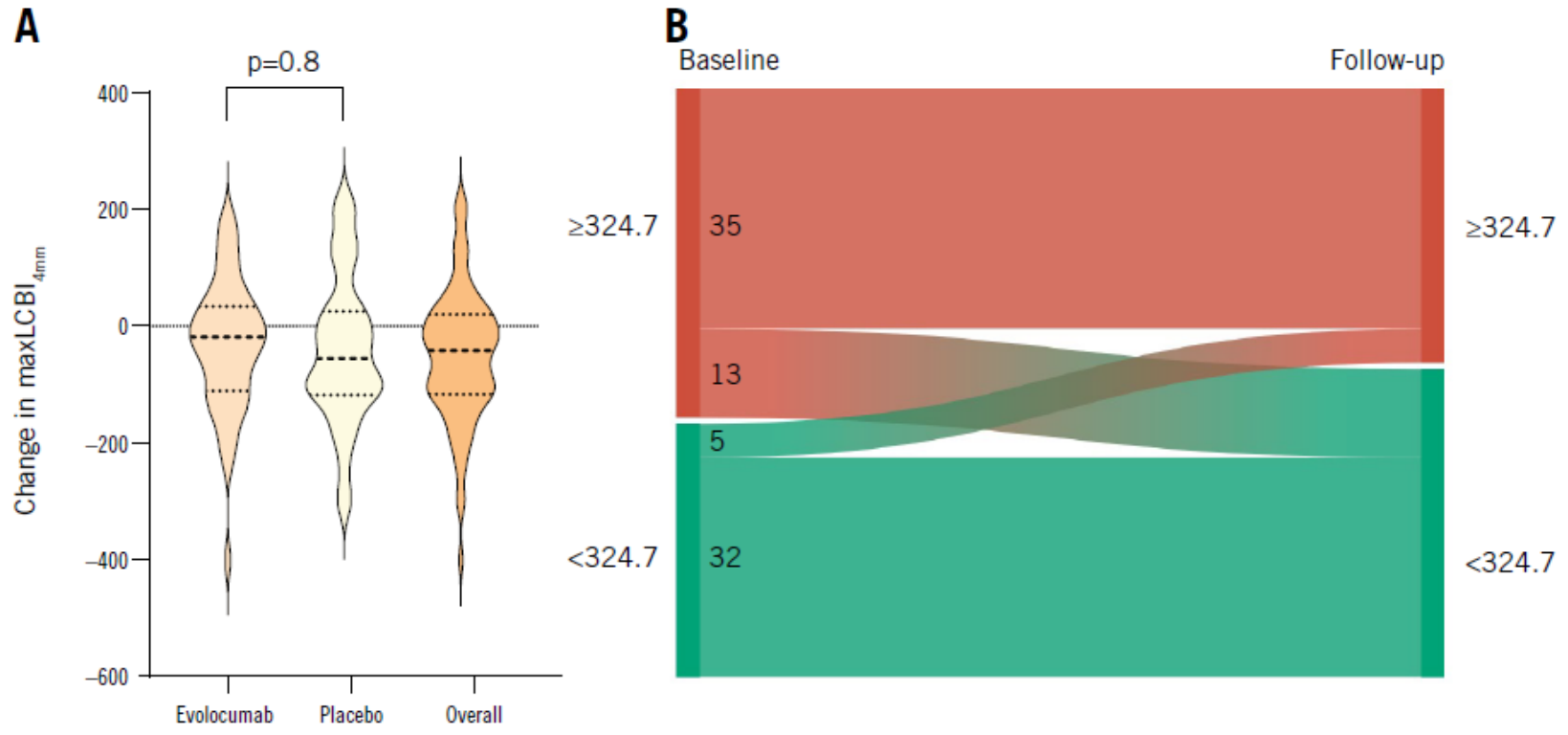
Mensink et al EuroIntervention. 2025 Aug 18;21(16):910-920

Treatment of high-risk plaques

Intensive LLT may not be sufficient in selected high-risk pts/lesions

The FITTER trial

Short-term effects of PCSK9i on functionally significant HRPs



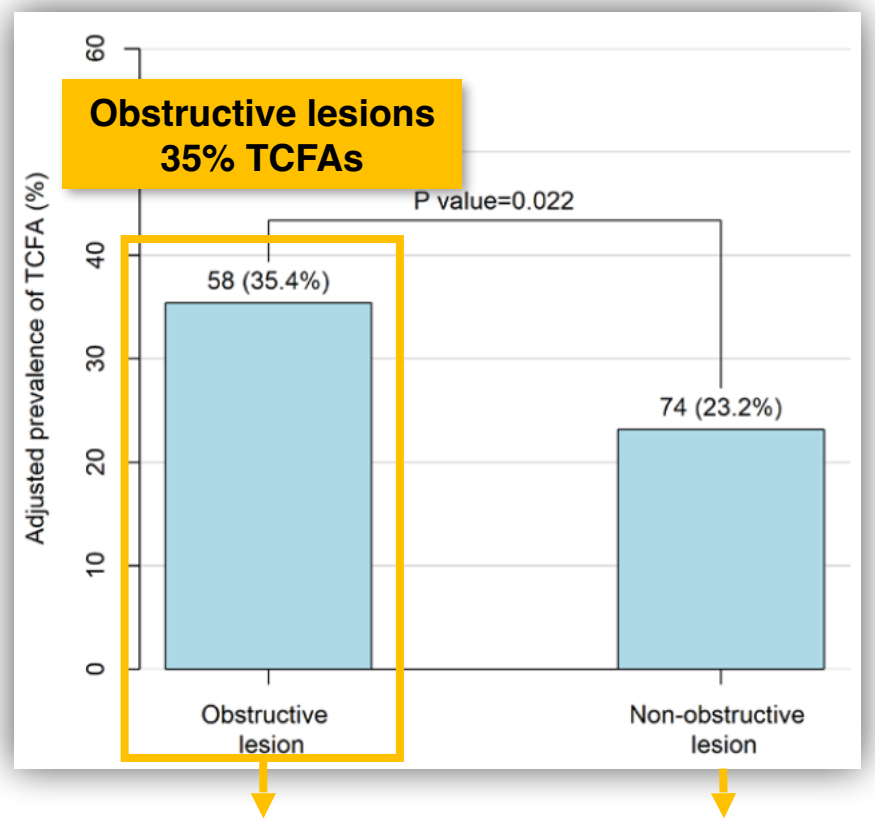
>40% stented at 3-month fup

Mensink et al EuroIntervention. 2025 Aug 18;21(16):910-920

Treatment of high-risk plaques

PCI for high-risk plaques: we already do it (in significant lesions)

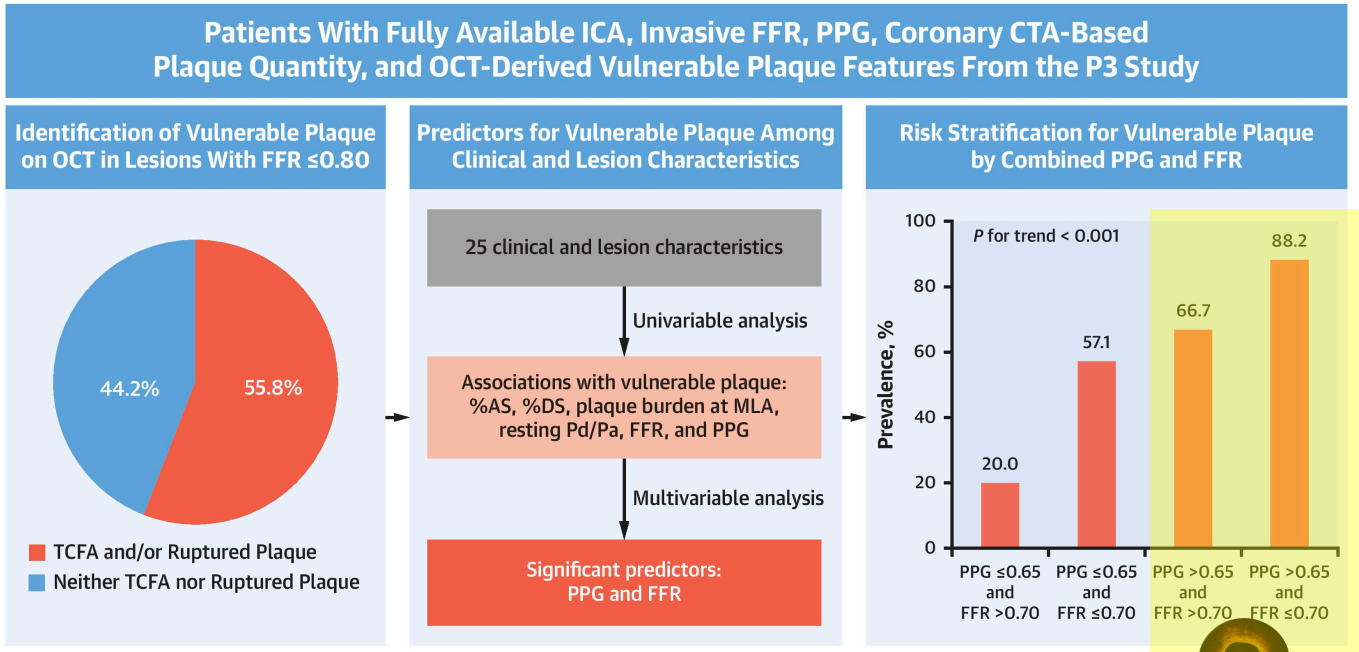
COMPLETE trial



Ischaemic lesions

Prevalence of vulnerable plaques in functionally significant lesions

CENTRAL ILLUSTRATION: Prediction of Vulnerable Plaque in Functionally Significant Lesions



Pinilla-Echeverri et al. Circ Cardiovasc Interv. 2020;13:e008768.

Yang et al. JACC Cardiovasc Imaging. 2025;18:195-206.

Treatment of high-risk plaques

Should we treat nonobstructive lesions with high-risk plaques?

Preventive focal therapy requirements:

1. Strong association with hard clinical events

↓

2. Safe focal treatment

↓

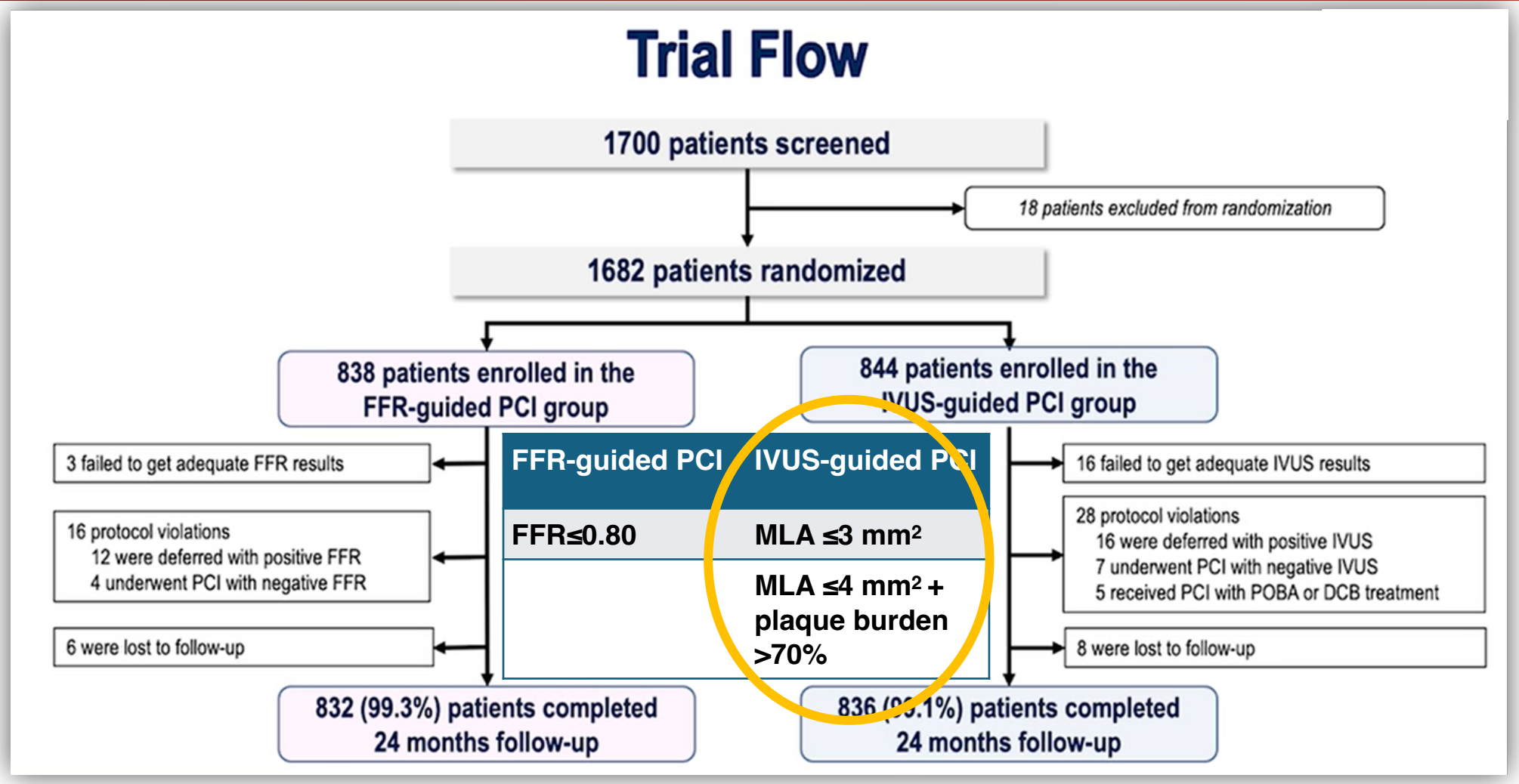
3. Clinically meaningful outcome reduction

↓

4. Cost-effective strategy

Treatment of high-risk plaques

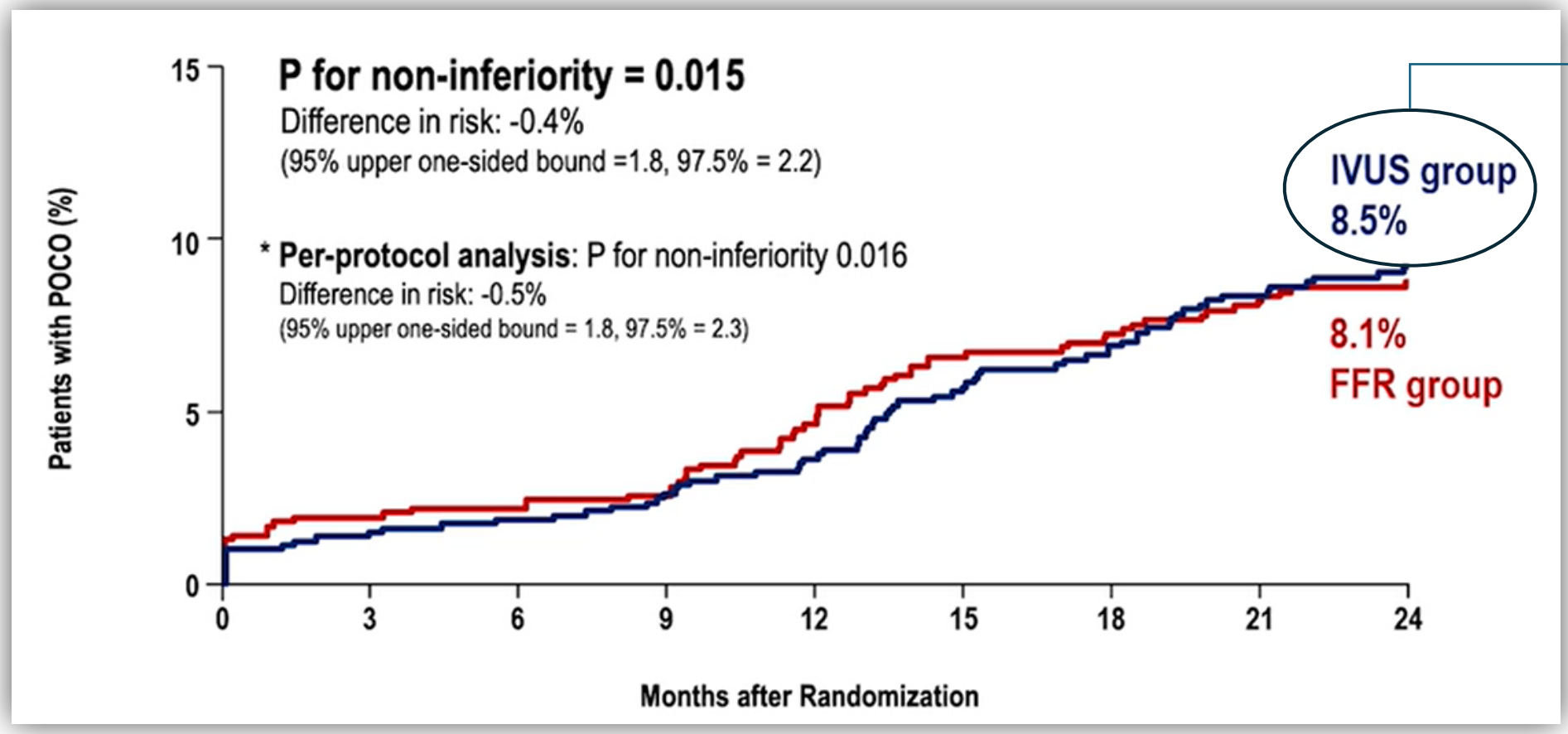
Invasive treatment of HRP #1: the FLAVOUR-AMI trial



Koo et al. N Engl J Med 2022;387:779-89.

Treatment of high-risk plaques

Invasive treatment of HRP #1: the FLAVOUR-AMI trial



- Mean plaque burden 70.1%
- Mean MLA 3.4 mm²

Death from any cause, MI, any revascularization

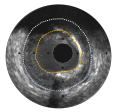
Treatment of high-risk plaques

Invasive treatment of HRP #2: the PREVENT trial

PREVENT TRIAL

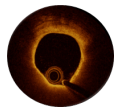
=limitations

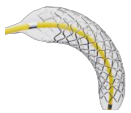
- 1606 pts with FFR-negative lesions
- 80% stable patients
- <2% on PCSK9i



Vulnerability features treated:

- 95% assessed by IVUS (plaque burden >70% and MLA <4 mm2
- Only 5% of OCT-derived TCFAs

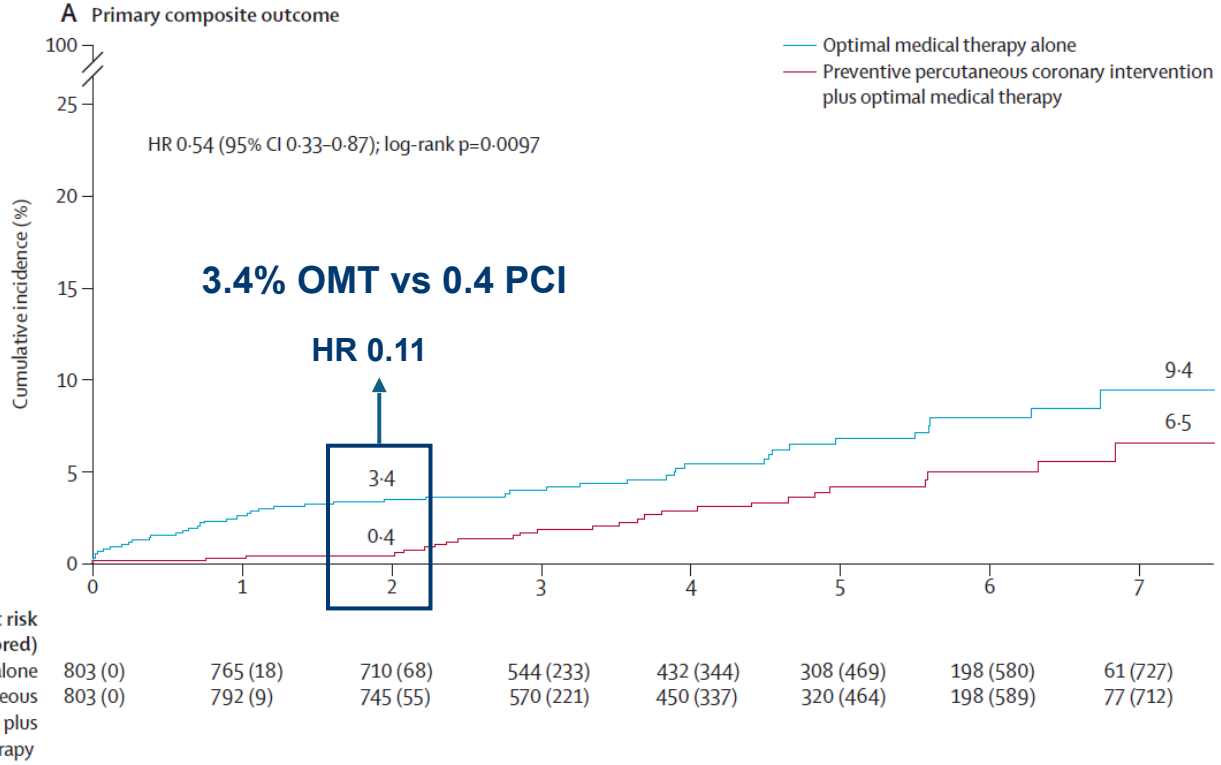




Focal therapy (729 stents):

- 67% DES
- 33% BVS absorb

Primary endpoint
MACE: CV death, TVMI, TVR, hospitalization for UA



Absolute reduction of 4 MIs and 1 cardiac death

Park et al. Lancet 2024;403:1753-1765

Treatment of high-risk plaques

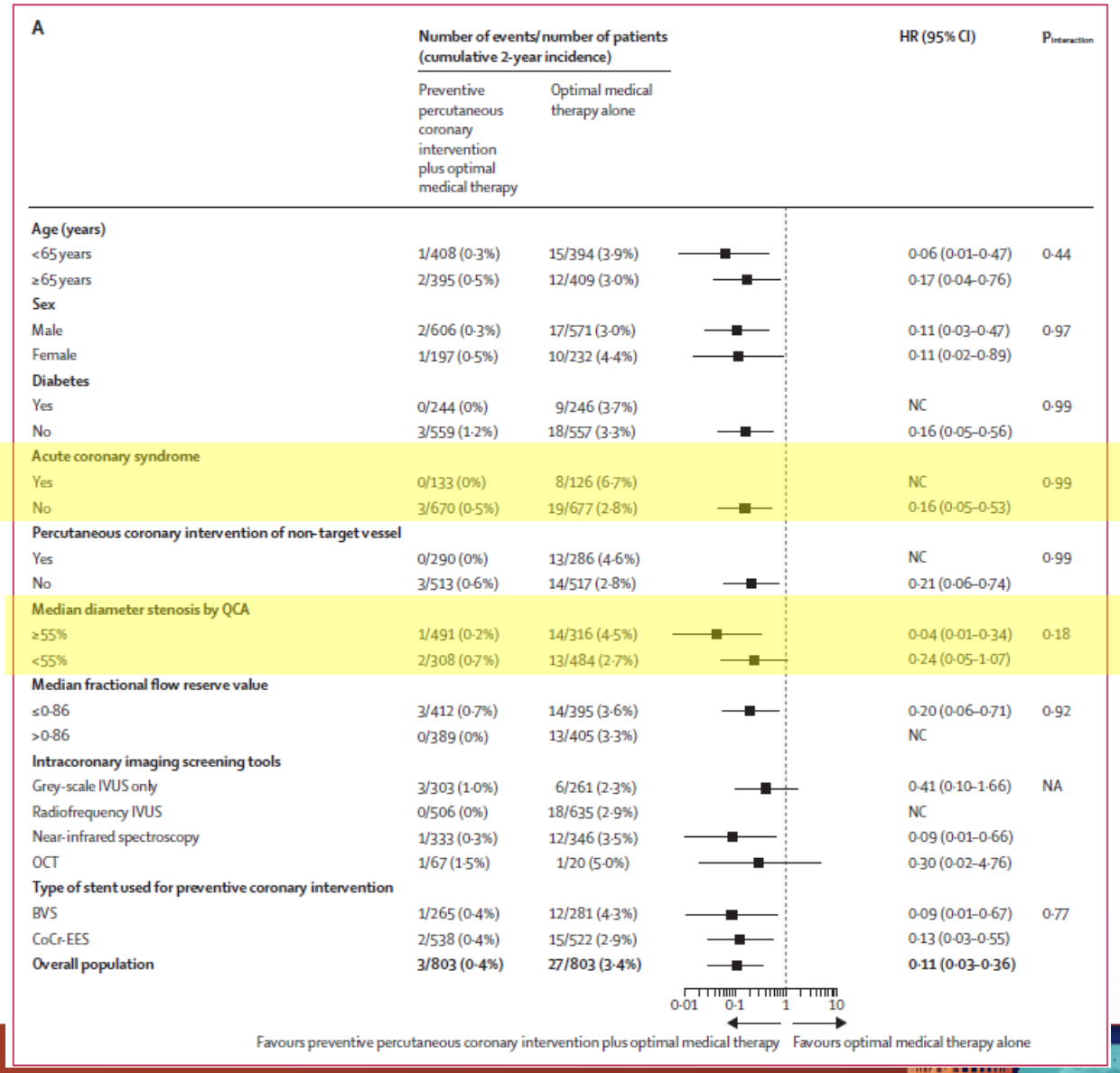
Invasive treatment of HRP #2: the PREVENT trial

Subgroup analyses

Greatest clinical benefit:

- **ACS**
  Pts with ACS had 0% events in the imaging group vs 6.7% in the OMT group

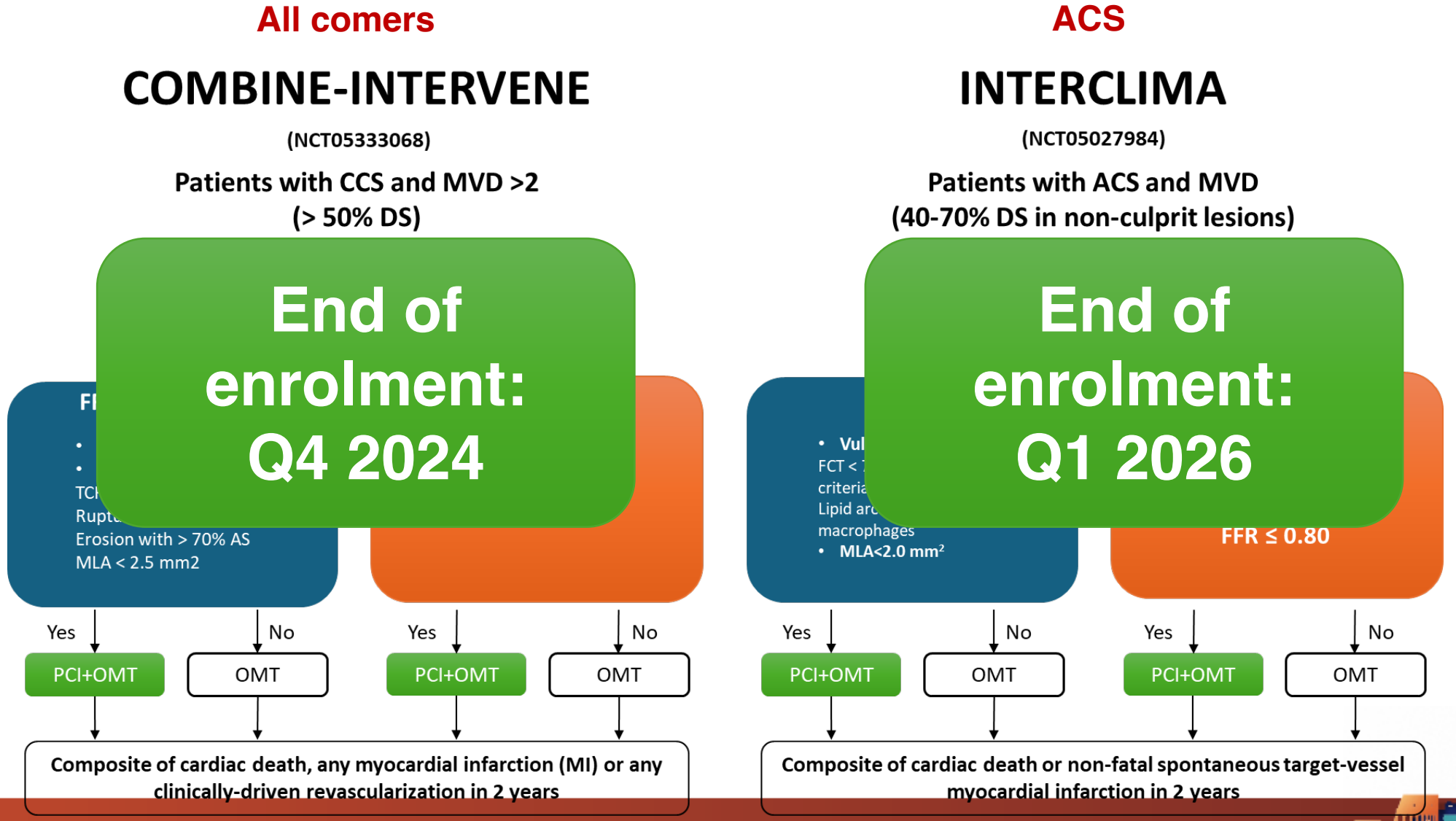
- **Stenosis >55%**
  HR 0.04 vs 0.24 in CCS



A	Number of events/number of patients (cumulative 2-year incidence)		HR (95% CI)	$P_{interaction}$
	Preventive percutaneous coronary intervention plus optimal medical therapy	Optimal medical therapy alone		
Age (years)				
<65 years	1/408 (0·3%)	15/394 (3·9%)	0·06 (0·01–0·47)	0·44
≥65 years	2/395 (0·5%)	12/409 (3·0%)	0·17 (0·04–0·76)	
Sex				
Male	2/606 (0·3%)	17/571 (3·0%)	0·11 (0·03–0·47)	0·97
Female	1/197 (0·5%)	10/232 (4·4%)	0·11 (0·02–0·89)	
Diabetes				
Yes	0/244 (0%)	9/246 (3·7%)	NC	0·99
No	3/559 (1·2%)	18/557 (3·3%)	0·16 (0·05–0·56)	
Acute coronary syndrome				
Yes	0/133 (0%)	8/126 (6·7%)	NC	0·99
No	3/670 (0·5%)	19/677 (2·8%)	0·16 (0·05–0·53)	
Percutaneous coronary intervention of non-target vessel				
Yes	0/290 (0%)	13/286 (4·6%)	NC	0·99
No	3/513 (0·6%)	14/517 (2·8%)	0·21 (0·06–0·74)	
Median diameter stenosis by QCA				
≥55%	1/491 (0·2%)	14/316 (4·5%)	0·04 (0·01–0·34)	0·18
<55%	2/308 (0·7%)	13/484 (2·7%)	0·24 (0·05–1·07)	
Median fractional flow reserve value				
≤0·86	3/412 (0·7%)	14/395 (3·6%)	0·20 (0·06–0·71)	0·92
>0·86	0/389 (0%)	13/405 (3·3%)	NC	
Intracoronary imaging screening tools				
Grey-scale IVUS only	3/303 (1·0%)	6/261 (2·3%)	0·41 (0·10–1·66)	NA
Radiofrequency IVUS	0/506 (0%)	18/635 (2·9%)	NC	
Near-infrared spectroscopy	1/333 (0·3%)	12/346 (3·5%)	0·09 (0·01–0·66)	
OCT	1/67 (1·5%)	1/20 (5·0%)	0·30 (0·02–4·76)	
Type of stent used for preventive coronary intervention				
BVS	1/265 (0·4%)	12/281 (4·3%)	0·09 (0·01–0·67)	0·77
CoCr-EES	2/538 (0·4%)	15/522 (2·9%)	0·13 (0·03–0·55)	
Overall population	**3/803 (0·4%)**	**27/803 (3·4%)**	**0·11 (0·03–0·36)**	

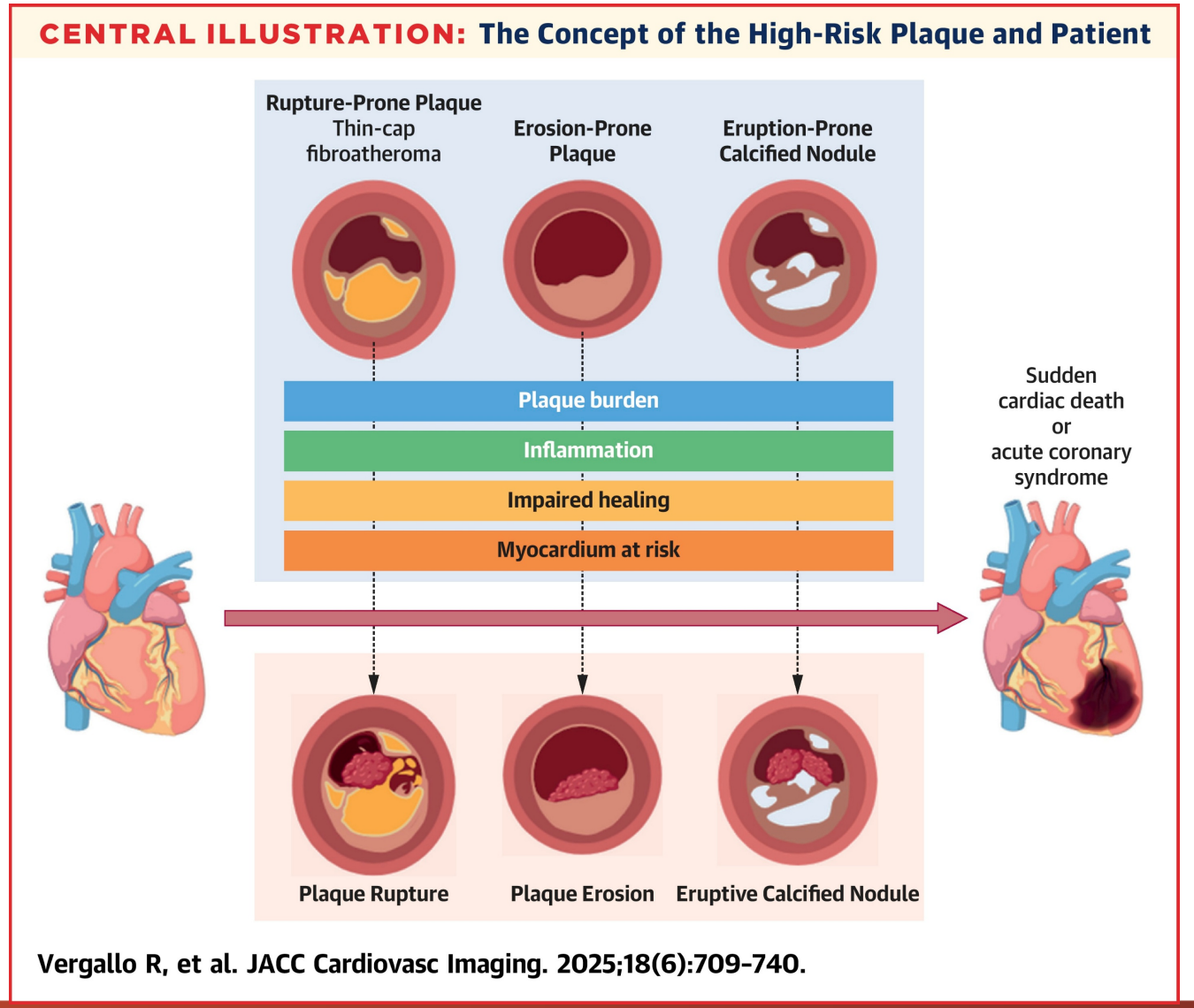
Treatment of high-risk plaques

Invasive treatment of HRP: ongoing large-scale randomised trials



Treatment of high-risk plaques

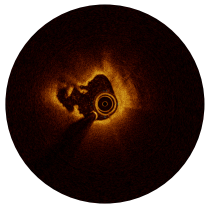
It is not all about TCFA



Vergallo R, et al. JACC Cardiovasc Imaging. 2025;18(6):709-740.

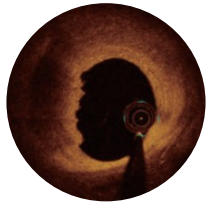
Lowering inflammation: two birds with one stone?

Plaque rupture



- TCFA
- Large necrotic core
- Fibrin-rich red thrombus

IFC thrombosis

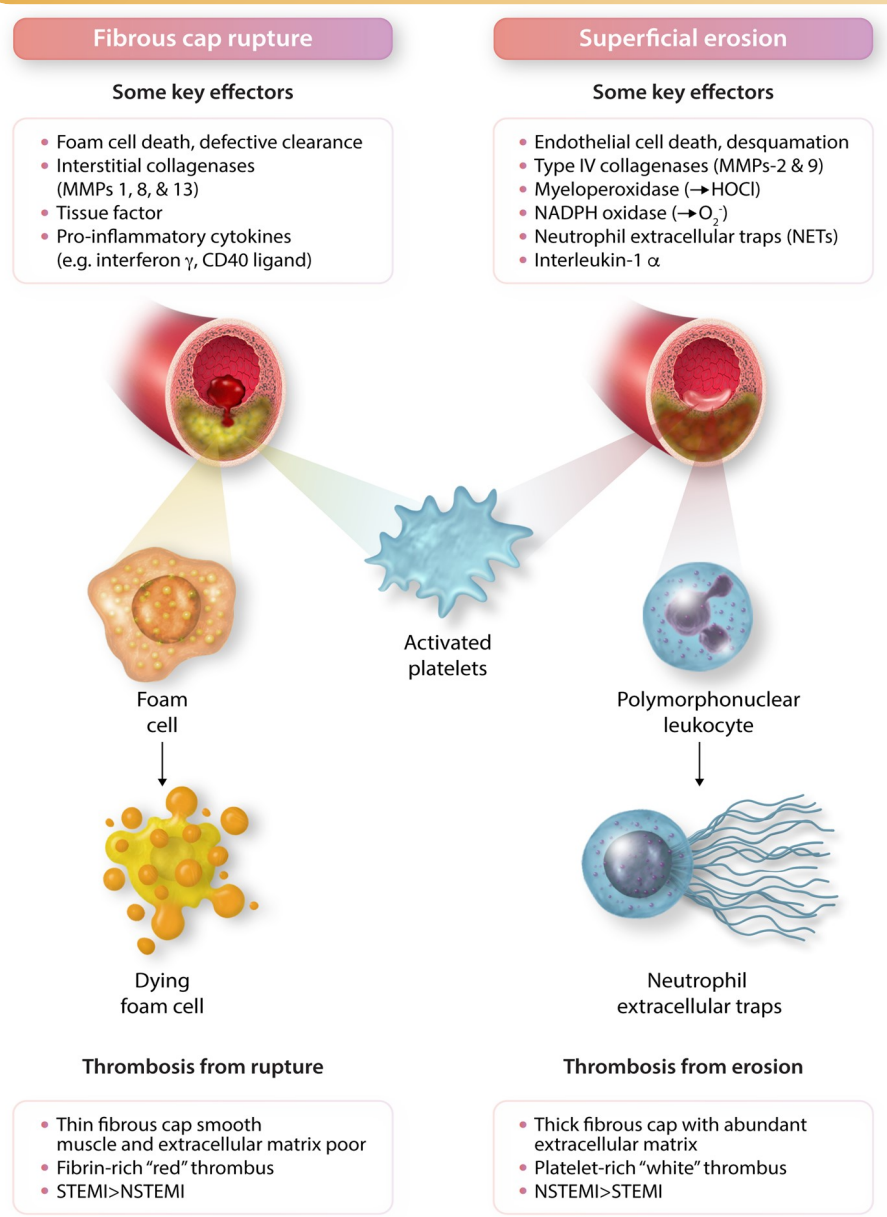


- Thick cap FA
- More fibro/calcific
- Platelet-rich white thrombus

Plaque rupture and IFC thrombosis have different morphological and pathophysiological mechanisms

Inflammation is shared by both

Distinct inflammatory pathways



Treatment of high-risk plaques

Invasive treatment of HRP

- **Intensive LLT remains the foundation of HRP management, yet a nonnegligible proportion of HRPs may persist, especially in advanced plaques**
- **Current evidence on preventive PCI of high-risk plaques is limited, largely IVUS-based, and not yet convincing enough**
- **Ongoing trials will clarify whether OCT-guided preventive DES-PCI can provide clinically meaningful benefit beyond optimal medical therapy**
- **Current knowledge does not allow to identify PE-prone lesions, which represent a substantial proportion of acute coronary event**
- **Future research is warranted to assess preventive PCI with devices designed to preserve or restore vessel morphology and pulsatility**