

# **The 29<sup>th</sup> TCTAP 2024**

**Vulnerable Plaque Treatment 2024**

**2024/4/26 (Fri), 2:50 PM ~ 2:58 PM, Main Arena, Level 2**

## **Vulnerable Plaque Stabilization With OMT: Lessons From Serial Imaging Studies**

**Takashi Kubo**

**Tokyo Medical University, Hachioji Medical center, Tokyo, Japan**

# Disclosure statement of financial interest

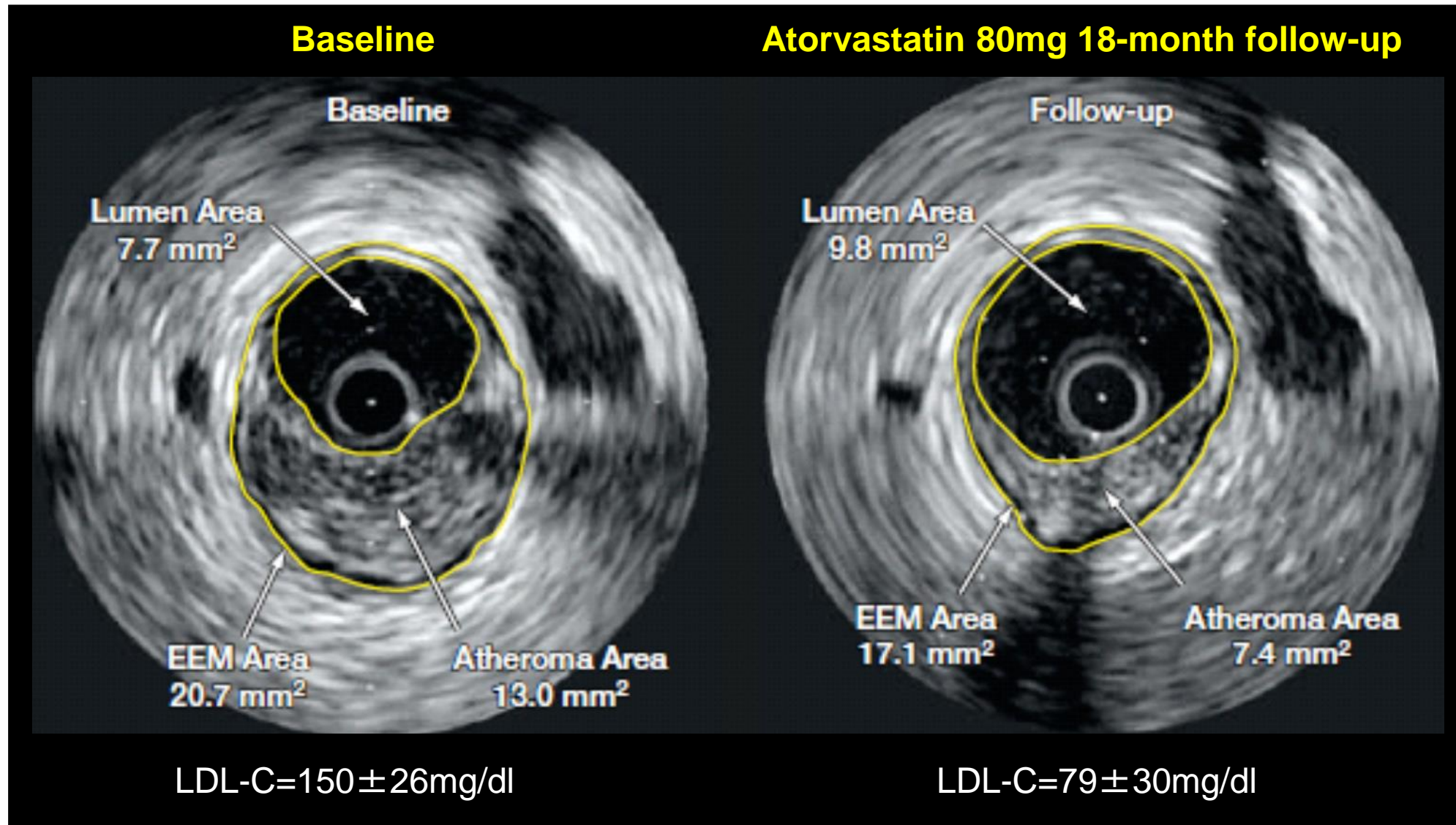
Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

## Affiliation/Financial Relationship

## Company

- |                                  |      |
|----------------------------------|------|
| • Grant/Research Support         | • No |
| • Consulting Fees/Honoraria      | • No |
| • Major Stock Shareholder/Equity | • No |
| • Royalty Income                 | • No |
| • Ownership/Founder              | • No |
| • Intellectual Property Rights   | • No |
| • Other Financial Benefit        | • No |

# IVUS: Decrease in plaque volume by statin



# OCT and NIRS: Increase in FCT and LCBI by PCSK9i

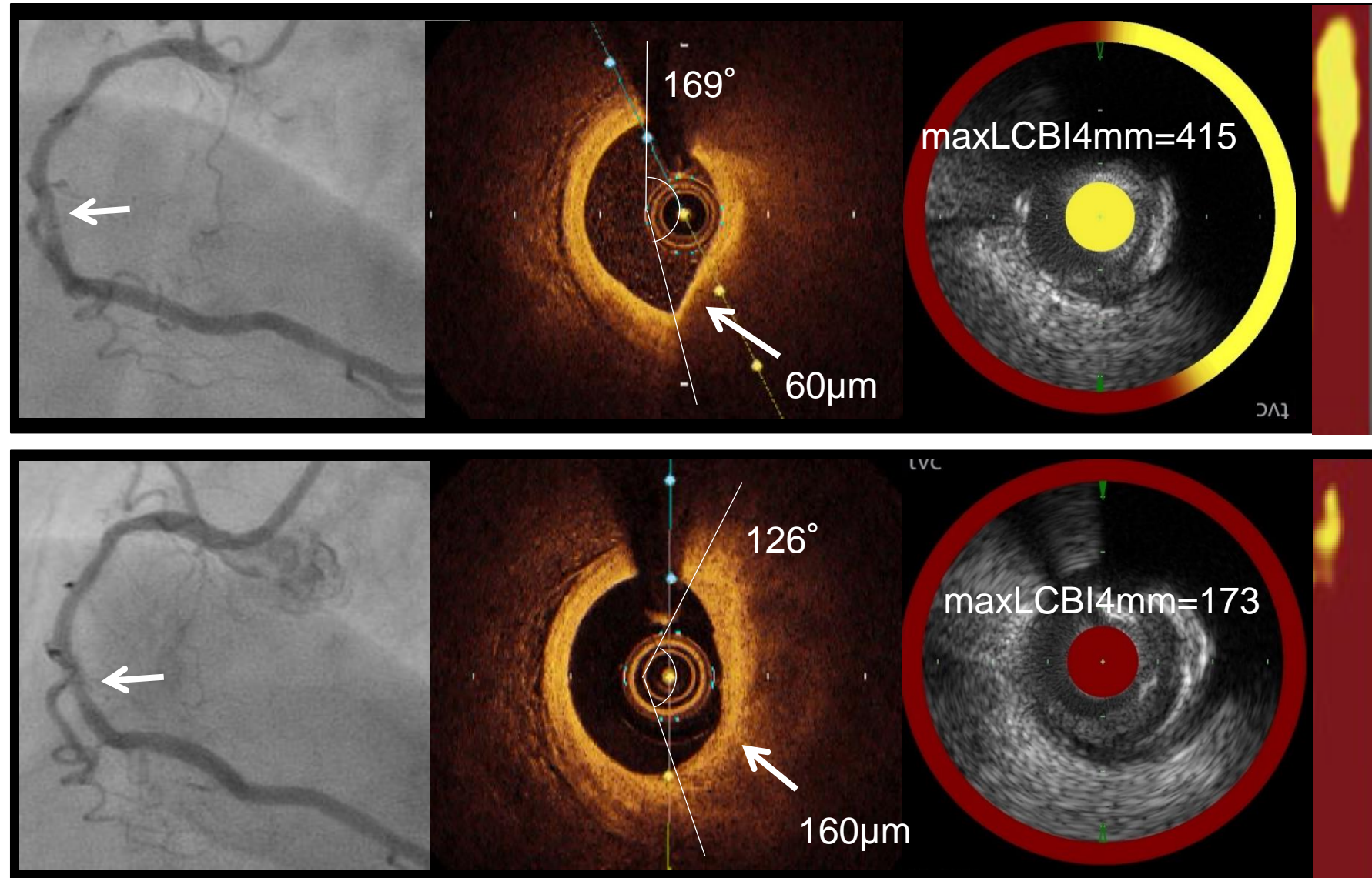
## Baseline

**LDL-C**  
**121mg/dl**

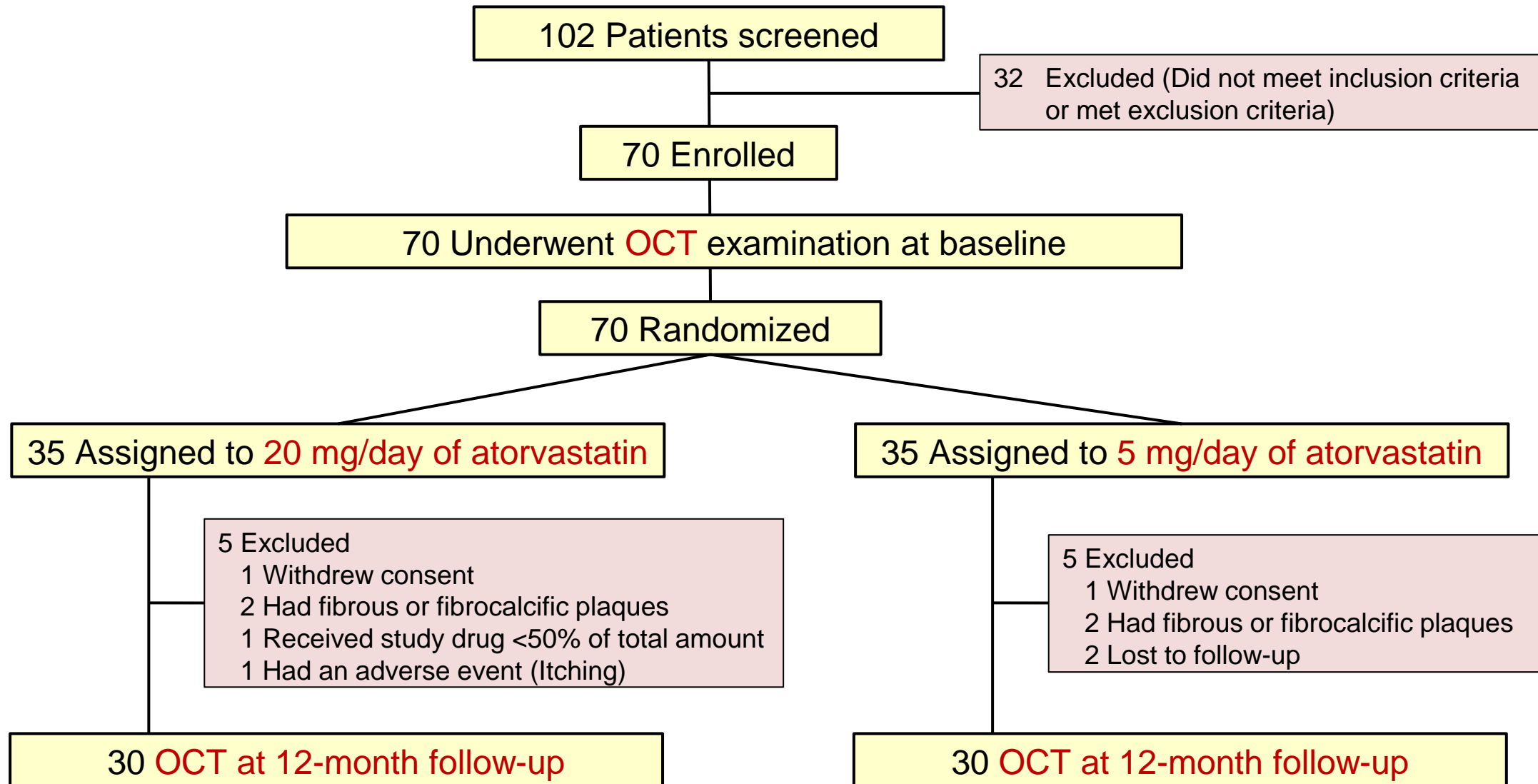
↓  
**Rosuvastatin**  
(10 mg/day)  
+  
**Evolocumab**  
(140 mg every 2 weeks)

## 8M follow-up

**LDL-C**  
**60mg/dl**

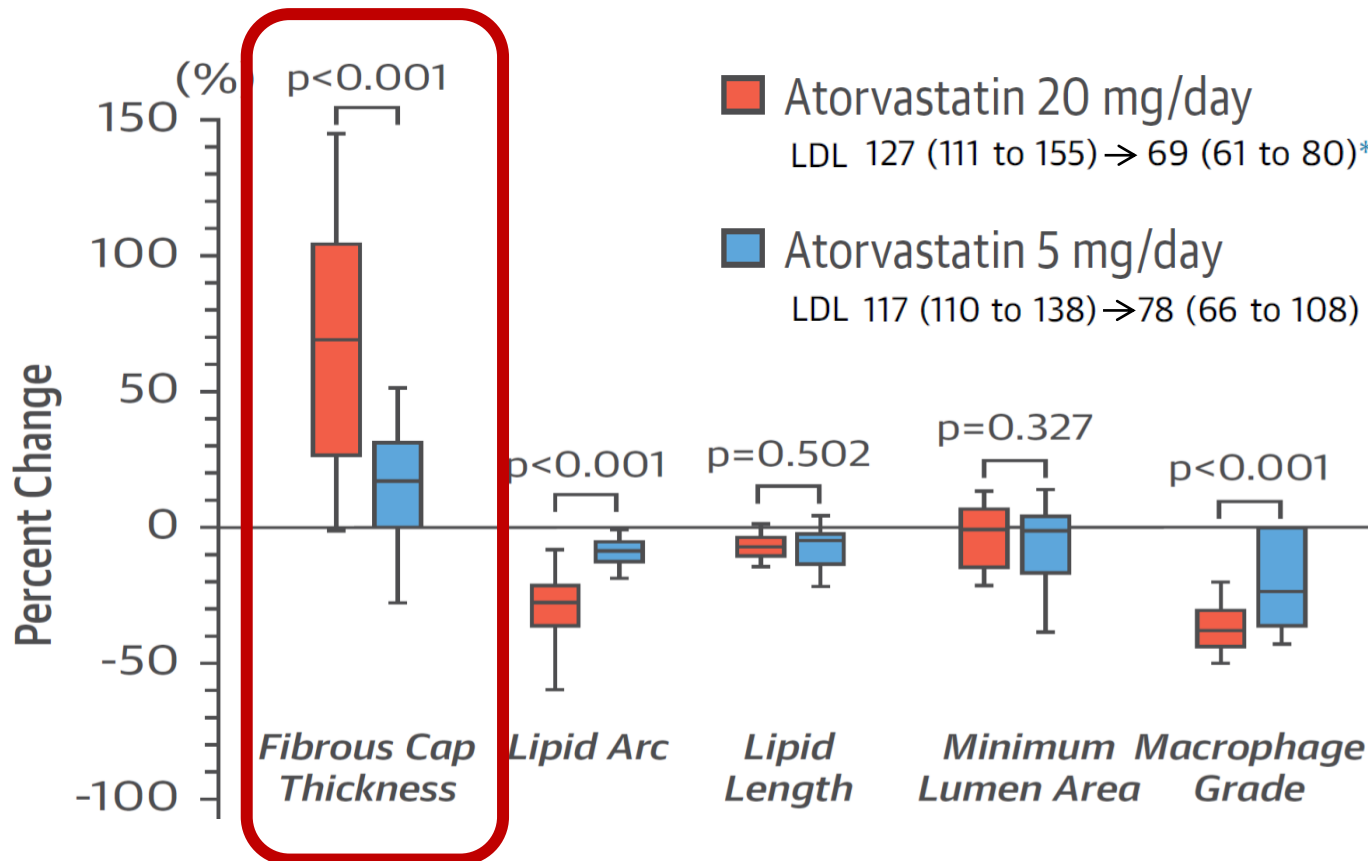
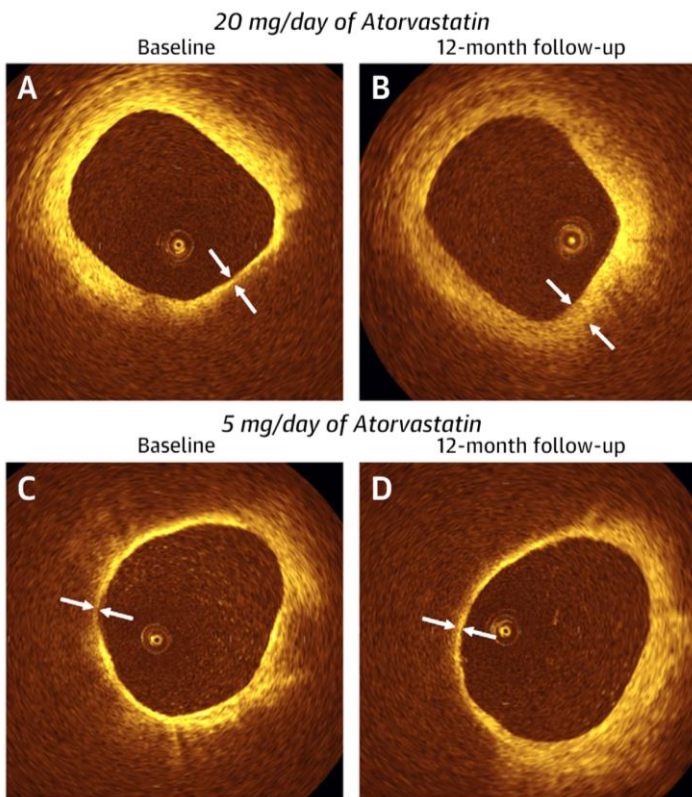


# EASY-FIT OCT trial: high-dose statin vs. low-dose statin



# Greater increase in FCT by high-dose statin

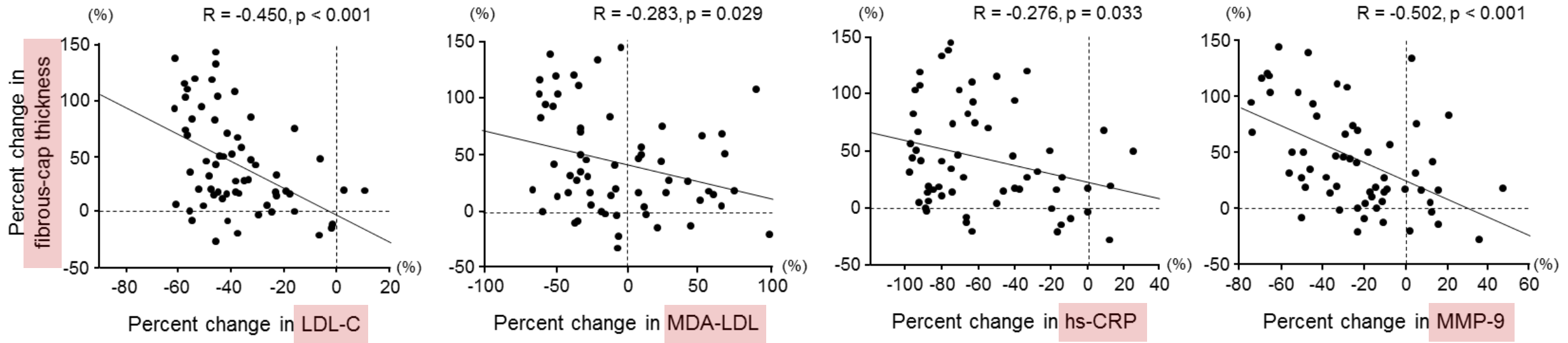
OCT was performed at baseline and 12M follow-up to assess the effect of lipid-lowering therapy with atorvastatin 20 mg/day vs atorvastatin 5 mg/day on fibrous cap thickness in coronary atherosclerotic plaque.



Atorvastatin 20 mg/day provided a greater increase in fibrous cap thickness in coronary plaques compared with atorvastatin 5 mg/day.

# Relationship between changes in biomarkers and FCT

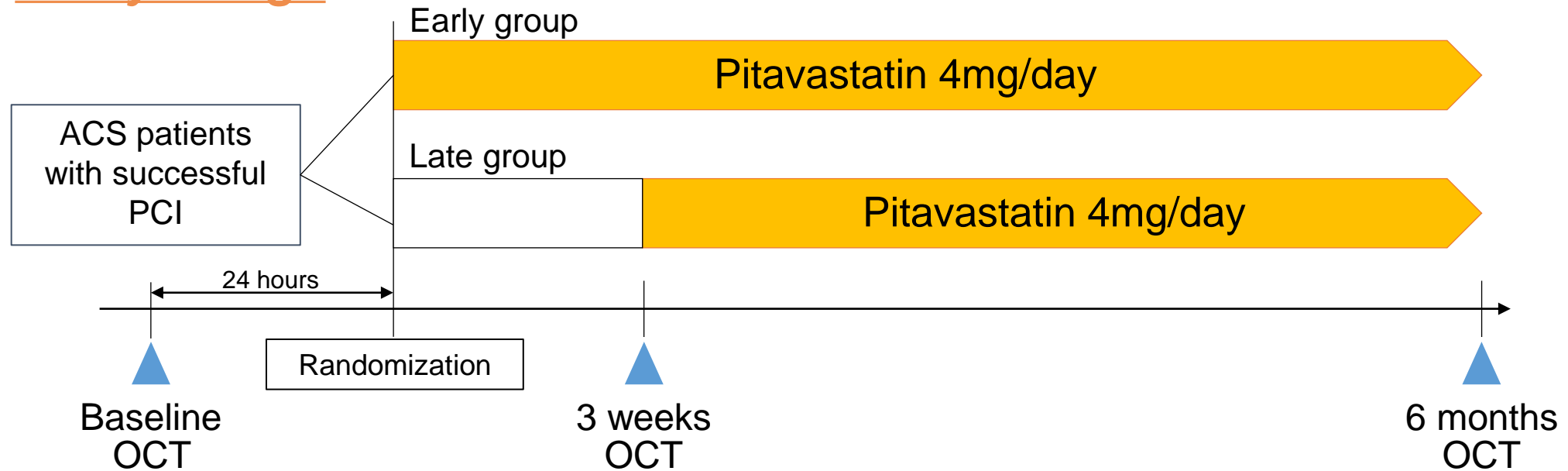
The relationship between the percentage of changes in biomarkers and in OCT-measured fibrous cap thickness during 12-month follow-up of lipid-lowering therapy with statin was assessed in 70 ACS patients.



The percent change in serum levels of LDL-C, MDA-LDL (Oxidized LDL), hs-CRP, and MMP-9 (that is produced by activated macrophages and induces collagen breakdown in the fibrous cap) was negatively correlated with the percent change in the fibrous cap thickness.

# ESCORT OCT trial: early statin vs. late statin

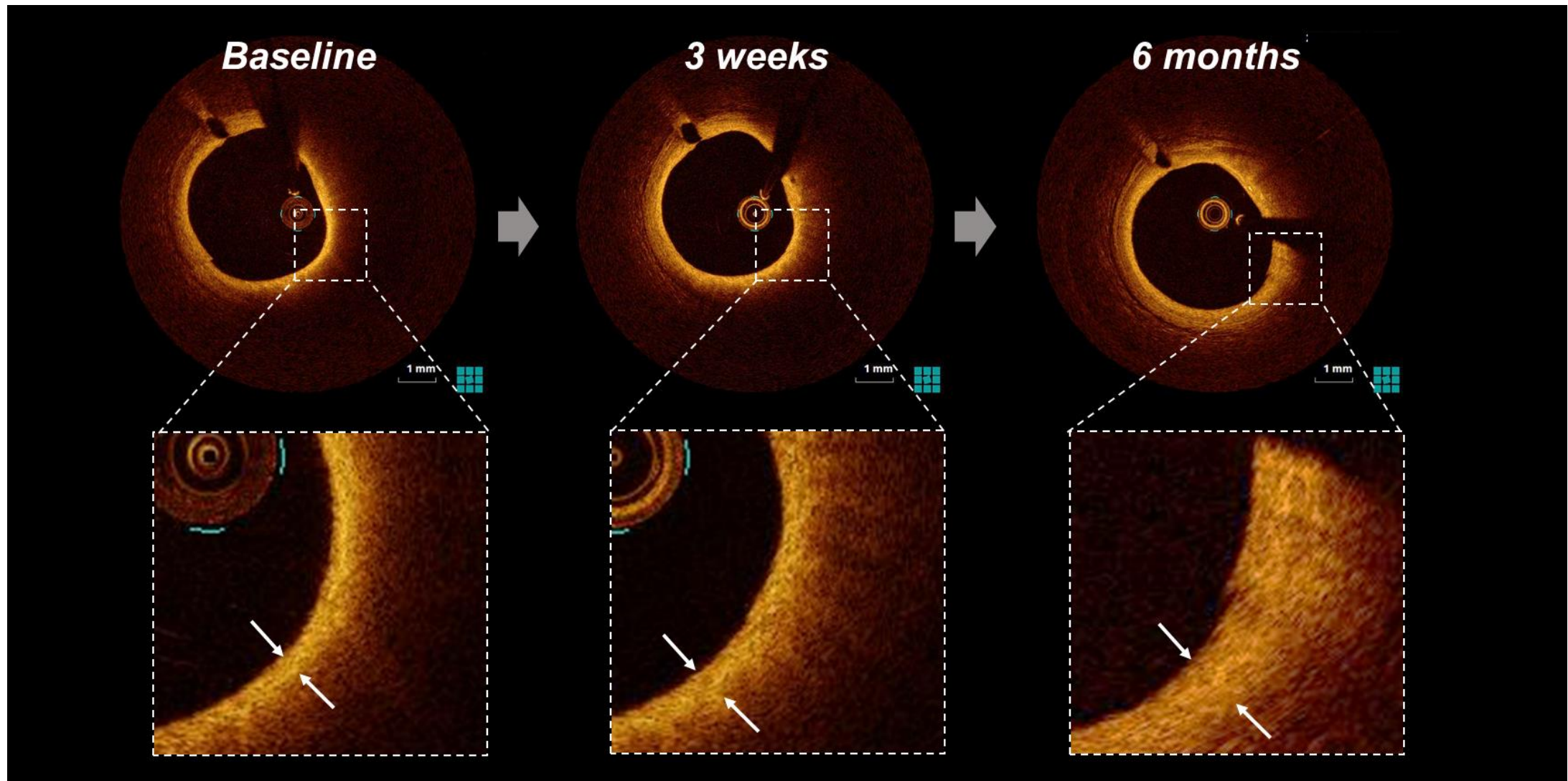
## Study design



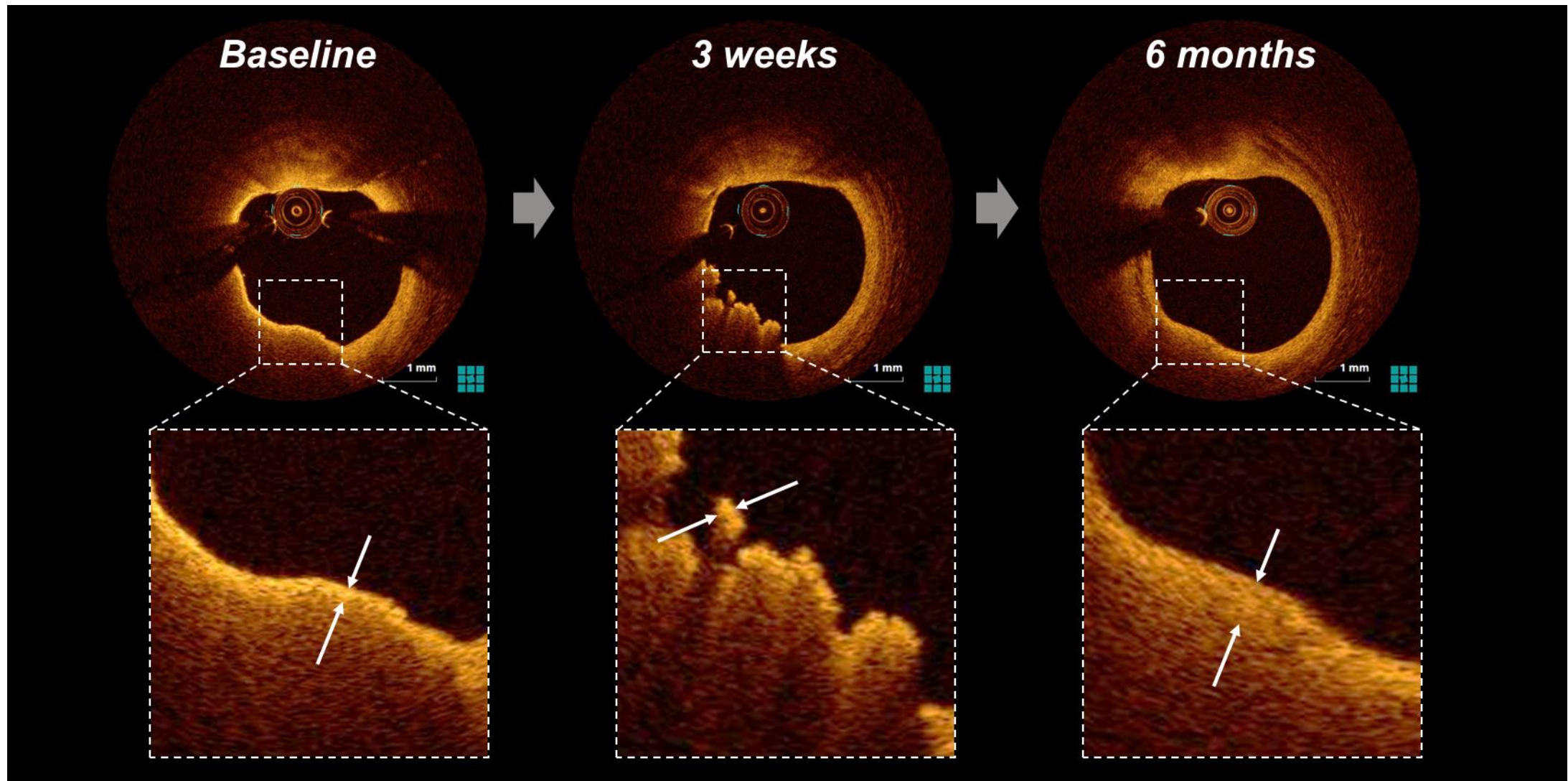
- 70 patients with ACS.
- LDL-Cholesterol level >100mg/dl at baseline.
- Patients were 1:1 randomized to early statin group (prescribing 4mg/day of pitavastatin on the day of admission) or late statin group (prescribing 4mg/day of pitavastatin after 3weeks).
- OCT was performed to assess fibrous-cap thickness (FCT) in non-culprit lesions at baseline, 3-week follow-up, and 6-month follow-up.



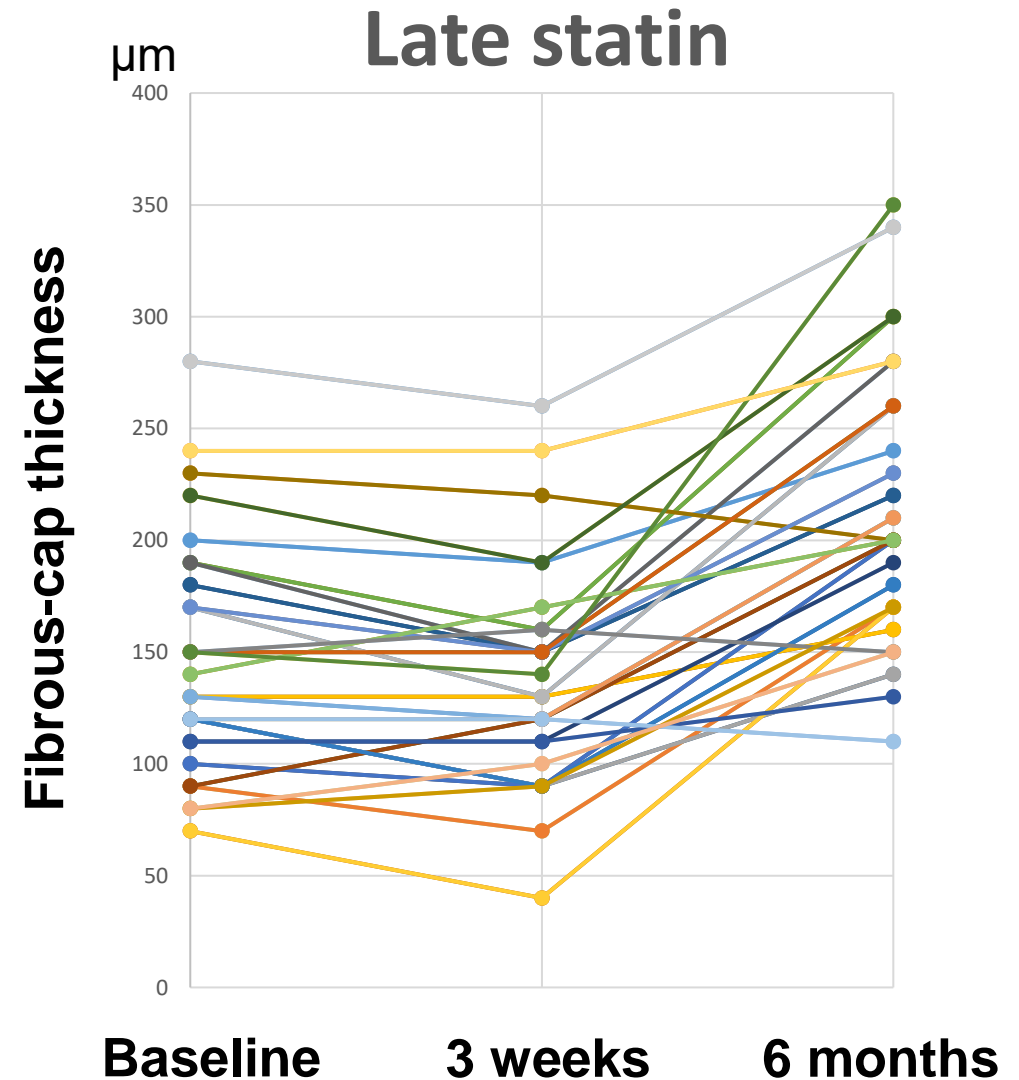
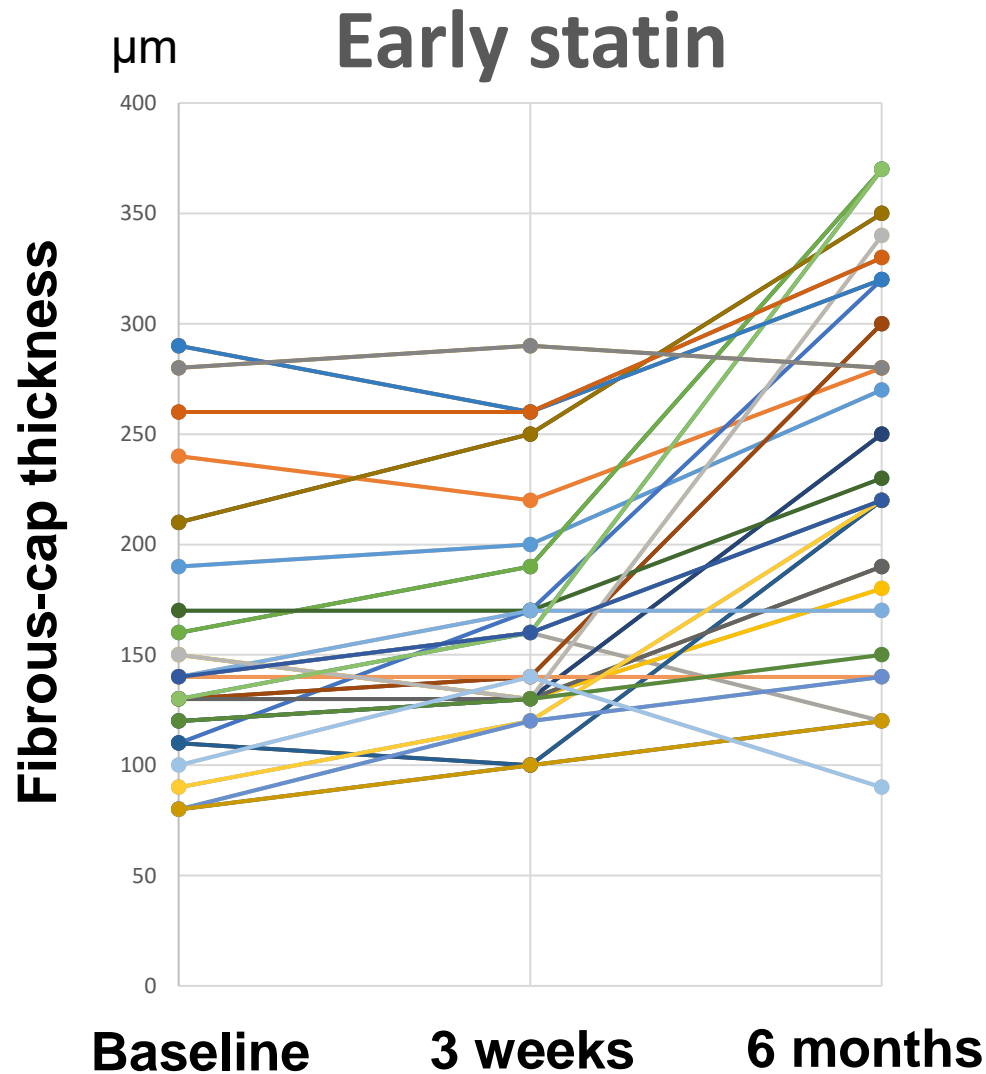
# Increase of FCT at 3W-FU in the early statin group



# FC disruption at 3W-FU in the late statin group

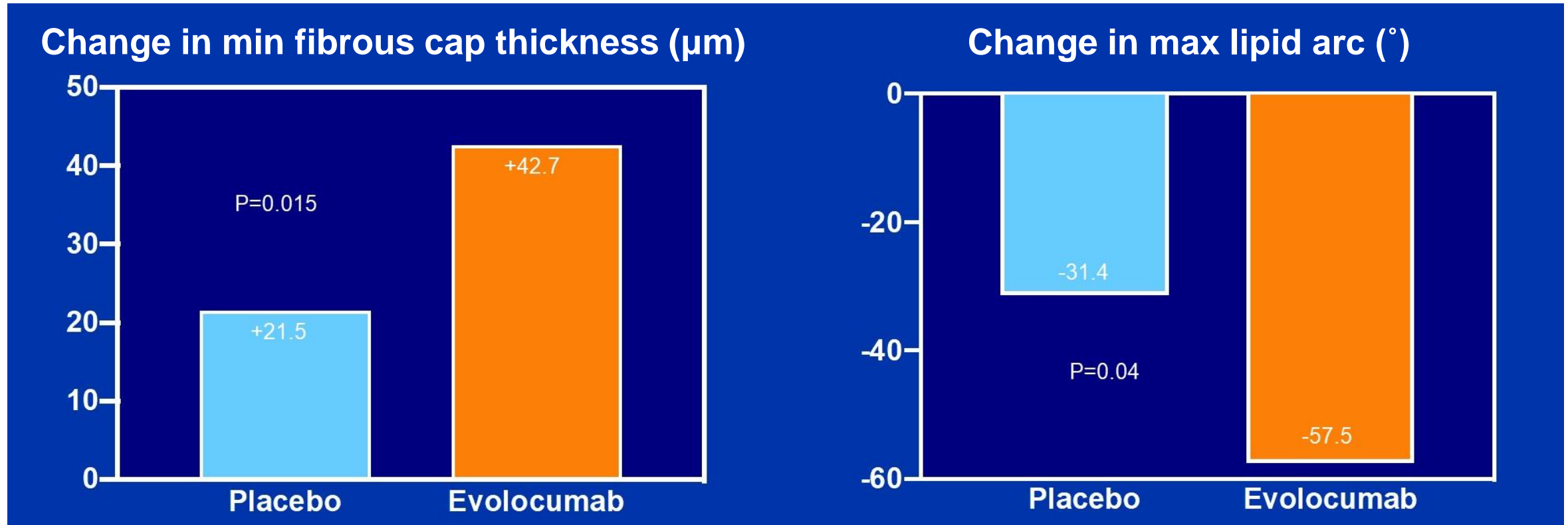


# FCT changes in early statin vs. late statin



# OCT: Increase in fibrous cap thickness by PCSK9i

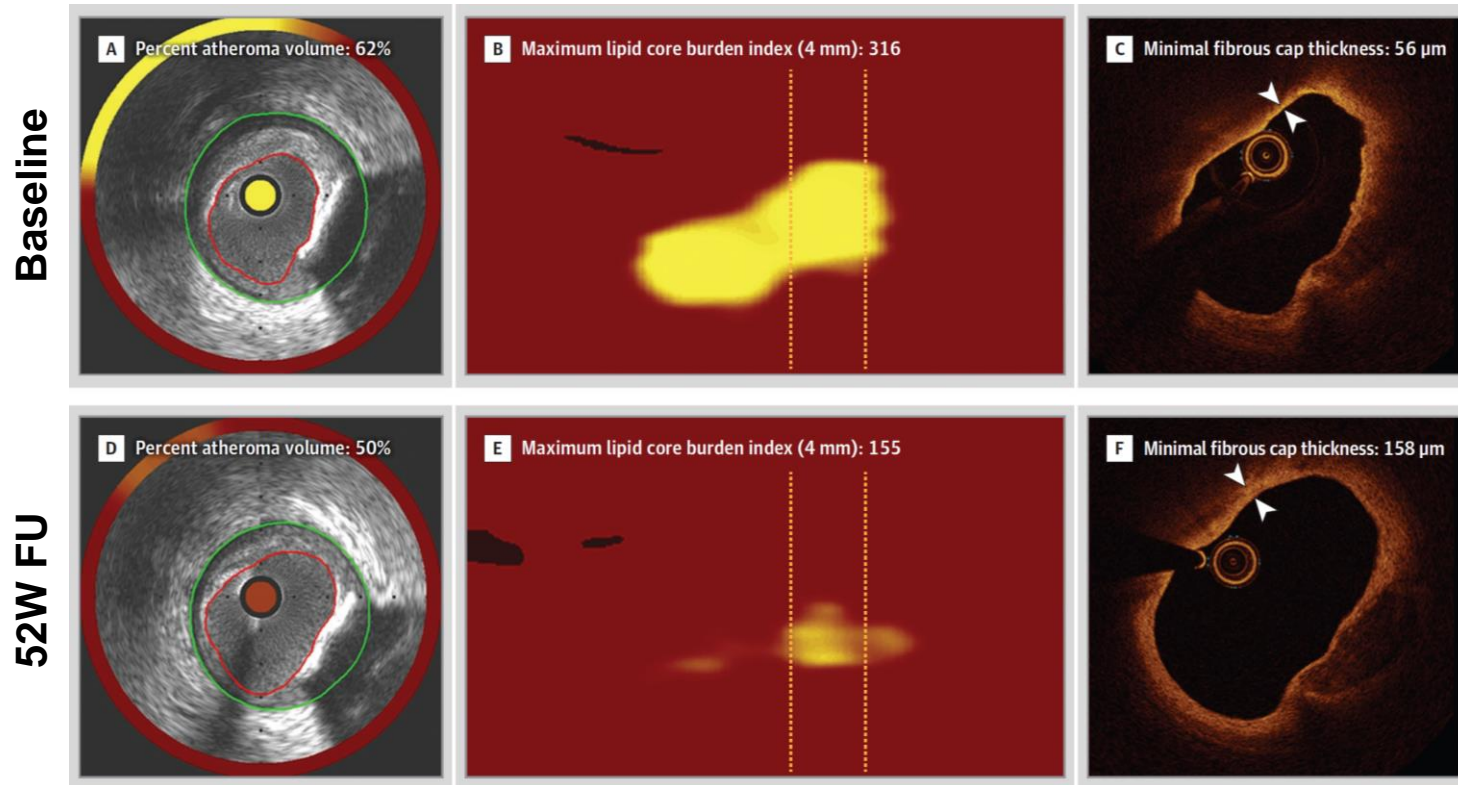
The **HUYGENS phase III study** is a multi-center, double-blind, RCT to evaluate the effect of PCSK9i evolocumab for 12 months on coronary atherosclerotic plaque by OCT in 161 patients with NSTEMI.



PCSK9i evolocumab resulted in greater increases in the minimum fibrous cap thickness and decreases in the maximum lipid arc compared with placebo.

# NIRS-IVUS: Decrease in maxLCBI(4) by PCSK9i

The **PACMAN-AMI study** used serial OCT and NIRS-IVUS at baseline and 52-week follow-up to determine the effects of PCSK9i alirocumab on coronary atherosclerosis in 300 patients with AMI.



For IVUS, external elastic lamina borders (green line) and lumen borders (red line) are superimposed and a reduction in percent atheroma volume from 62% to 50% is indicated.

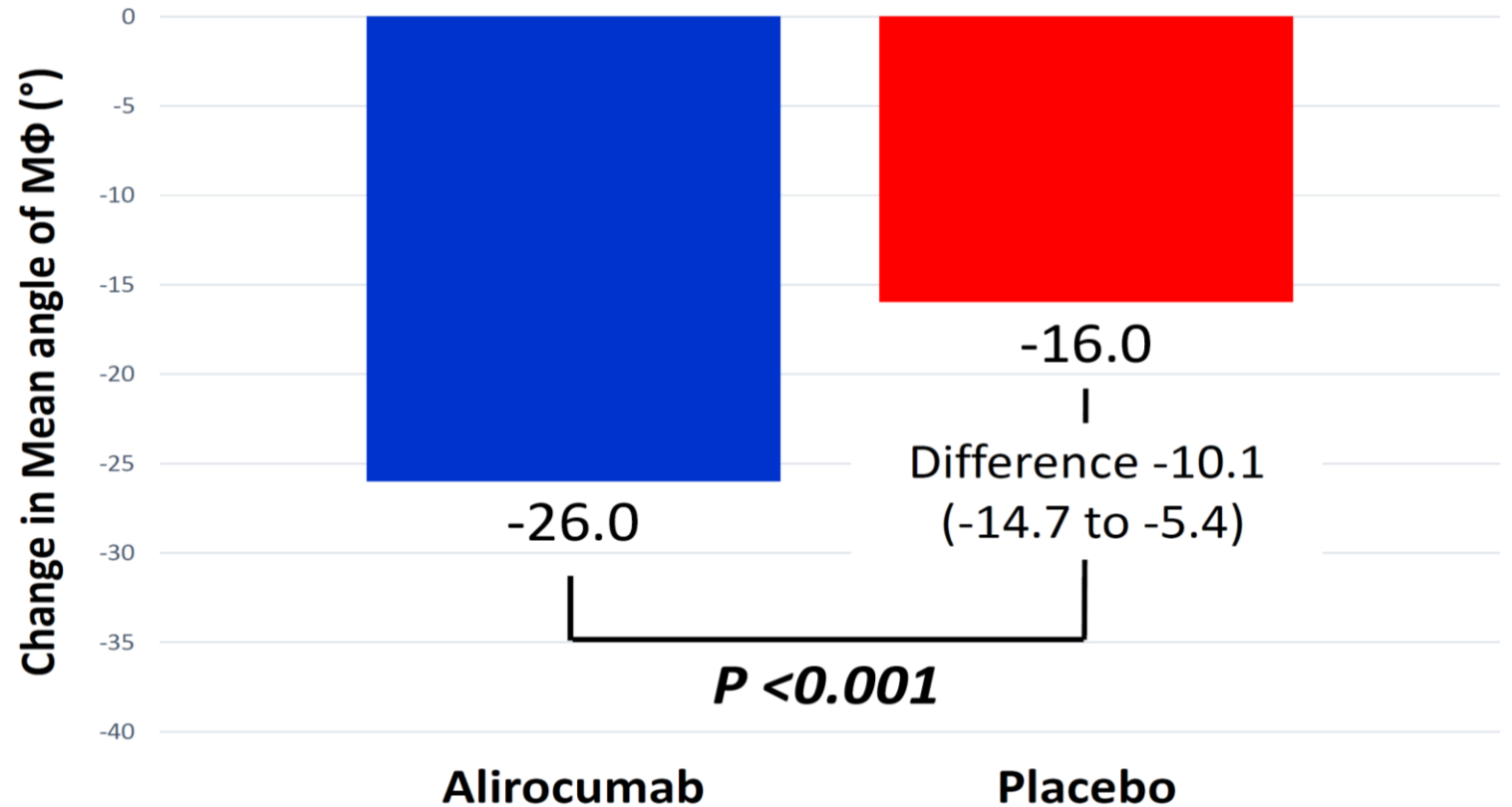
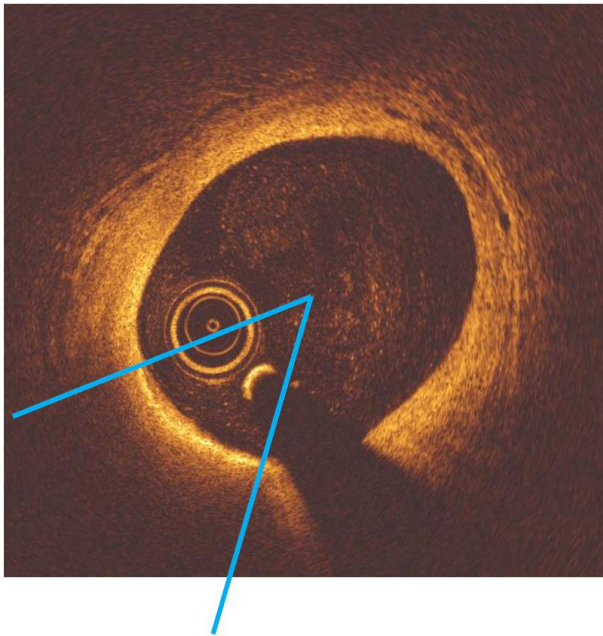
For NIRS, a reduction in maxLCBI4mm was measured; the dotted lines in panels B and E indicate the 4-mm region with greatest lipid accumulation.

For OCT, an increase in minimal fibrous cap thickness (noted by white arrows in panels C and F) from 56  $\mu\text{m}$  to 158  $\mu\text{m}$  was measured.

Alirocumab significantly reduced atheroma volume and maxLCBI(4) and significantly increased minimal fibrous cap thickness compared with placebo.

# OCT: Decrease in macrophages by PCSK9i

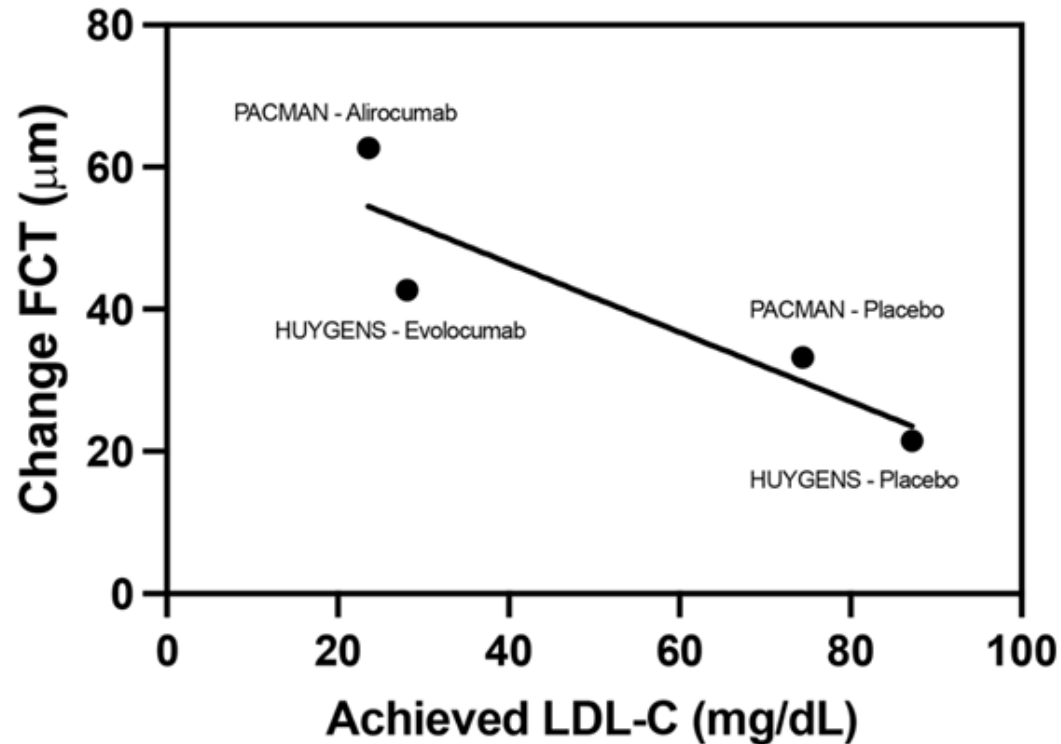
The **PACMAN-AMI study** used serial OCT and NIRS-IVUS at baseline and 52-week follow-up to determine the effects of PCSK9i alirocumab on coronary atherosclerosis in 300 patients with AMI.



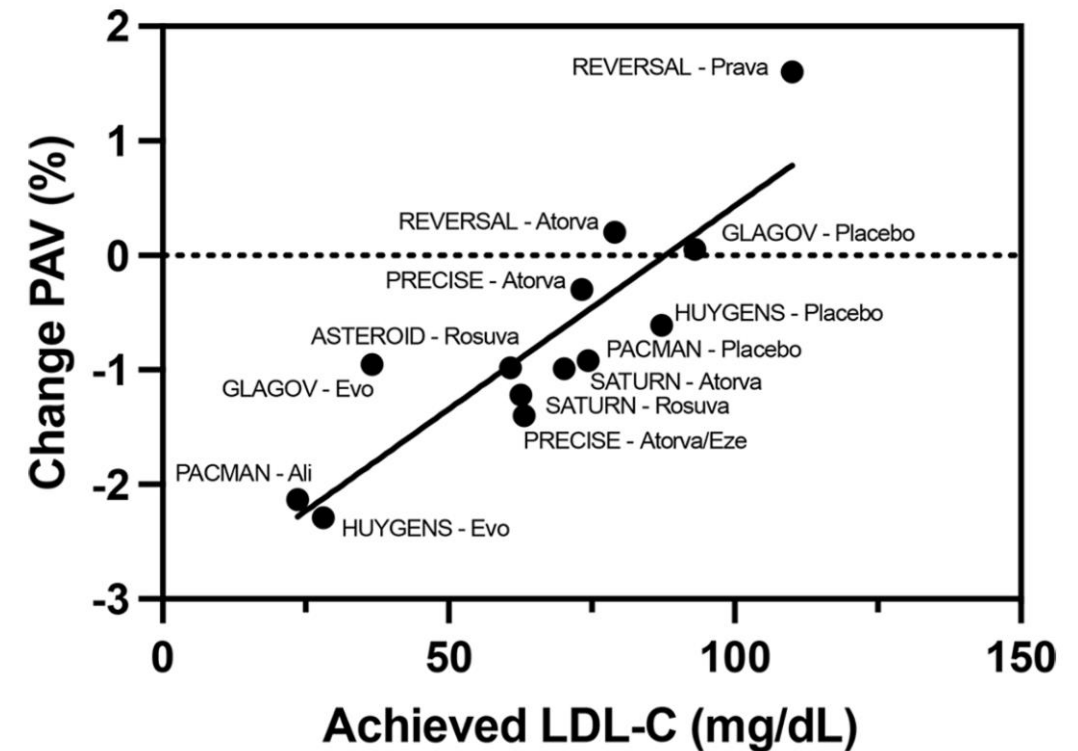
Alirocumab significantly reduced mean angular extension of macrophages compared with placebo.

# Effect of lipid lowering on FCT and plaque volume

## Fibrous-cap thickness (OCT)



## Plaque volume (IVUS)



OCT trials have shown a direct association between achieved LDL-C levels and changes in fibrous cap thickness. IVUS trials have shown that significant reductions in LDL-C levels achieved by more intensive lipid-lowering regimens lead to greater plaque regression.

# Conclusion

Serial intravascular imaging allows the observation of vulnerable plaque stabilization characterized by decreased atheromatous plaque volume, decreased lipid core, increased fibrous cap thickness, and decreased macrophage infiltration.