

*Atorvastatin Leads to Stabilization and
Regression of Coronary Plaque Trials
-Evaluation With Simultaneous Angioscopic and
Intravascular Ultrasound Examination-
(TWINS STUDY)*

Nihon University School of Medicine, Tokyo
Osaka Police Hospital, Osaka

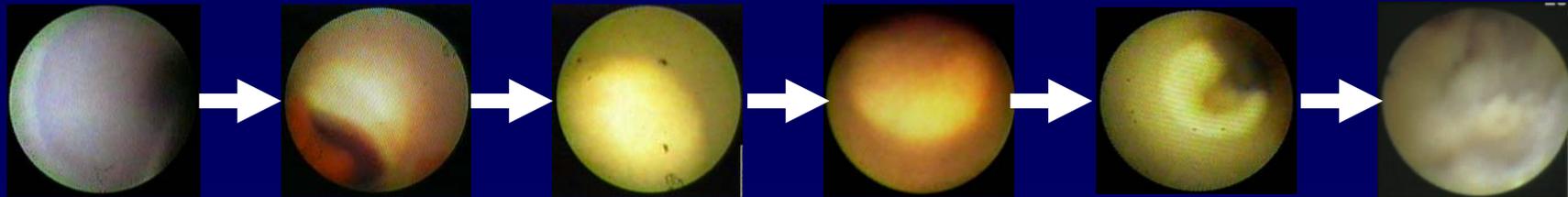
Division of Cardiology, Nihon University School of Medicine

Background

- ✓ **Lipid lowering therapy with statins reduces the cardiac events via plaque modification shown by the intravascular ultrasound (IVUS) and angioscopy.**
- ✓ **IVUS examination suggested the regression or prevention of the progression of plaque.**
- ✓ **Angioscopic examination showed the change in plaque color.**
- ✓ **However, there were no studies to reveal the effect of statins on plaque modification using both IVUS and angioscopy.**

Background (continued)

- ✓ **IVUS can measure the plaque volume to evaluate the progression or regression.**
- ✓ **Coronary angioscopic observation revealed that plaque with the increased yellow color became more vulnerable, then ruptured. So, coronary angiосcopy can assess the plaque surface to evaluate the stability.**



Objectives

To study the serial changes in coronary plaques by using IVUS and coronary angioscopy , then reveal the mechanism of the reduction of cardiac events by statins.

Study organization

Principal Investigator

Kazuhisa Kodama

Cardiovascular Division, Osaka Police Hospital

Study Center

- **Osaka Police Hospital** (Atsushi Hirayama, Yasunori Ueda)
- **Division of Cardiovascular Medicine Department of Medicine, Nihon University School of Medicine** (Tadateru Takayama, Junko Honye, Yuxin Li, Satoshi Saitoh)

Angioscopic Findings Review Board

Shinsuke Nanto Cardiovascular division, Kansai Rosai Hospital

Osamu Yamaguchi Department of Cardiovascular Medicine, Osaka University Graduate School of Medicine

IVUS Analysis Review Board

Kenji Takazawa Department of Cardiology, Tokyo Medical University Hachioji Medical Center

Junji Yajima Department of Internal Medicine, The Cardiovascular Institute Hospital

Patients' selection

Inclusion criteria

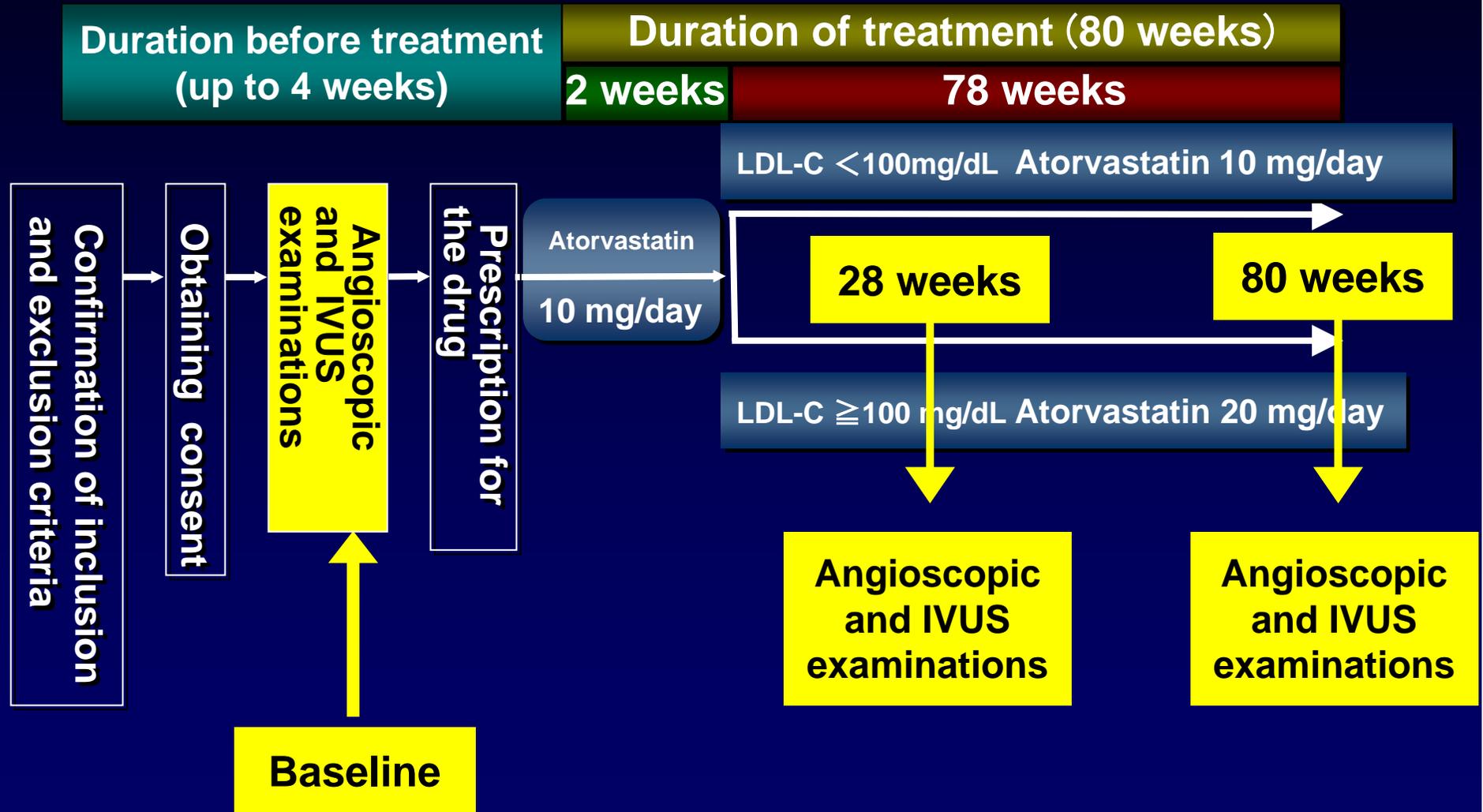
- ✓ Age ; 20-75 year olds
- ✓ Coronary heart disease
- ✓ LDL-cholesterol ≥ 120 mg/dL within 8 weeks before the initial administration of 10mg of Atorvastatin.
- ✓ Coronary artery with at least one yellow plaque with grade 2 or higher grade observed by angiography

Patients' selection

Exclusion criteria (major)

- ✓ Acute myocardial infarction within 24hours
- ✓ Contraindication of statin
- ✓ Uncontrolled diabetes mellitus (HbA1c \geq 8.0)
- ✓ Others

Study Protocol



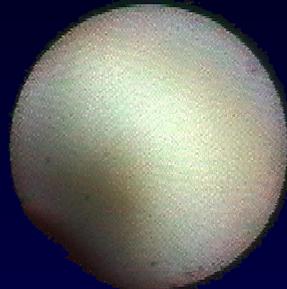
Primary efficacy assessment

- ✓ **Changes in plaque morphology observed by angioscopy (judged by angioscopic finding Review Board)**
- ✓ **Changes in plaque volume and echogenicity by IVUS (judged IVUS Analysis Review Board)**

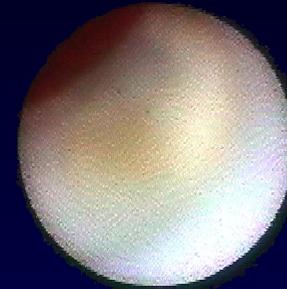
Assessment of angioscopic findings



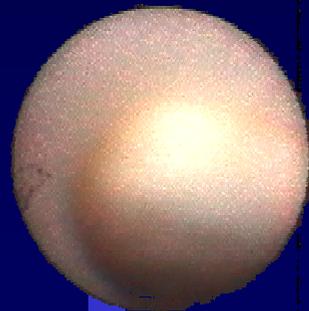
Grade 0
no yellow



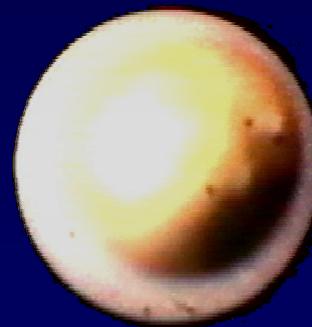
Grade 1
pale yellow plaque



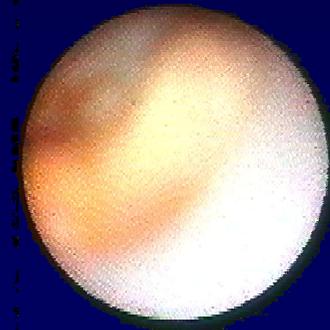
Grade 2
yellow plaque



Grade 3
intensive yellow plaque

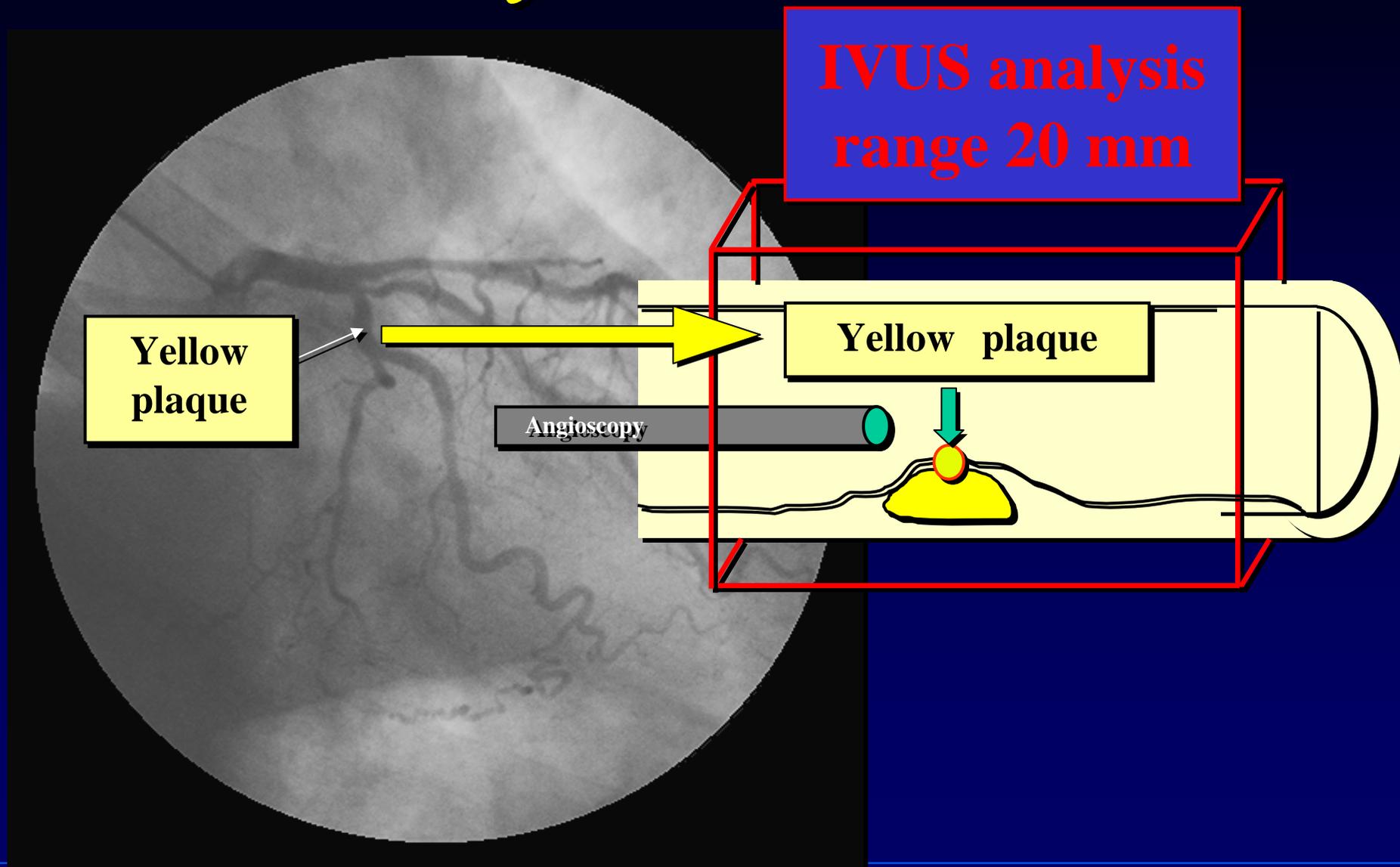


Grade 4
Glittering yellow plaque



Grade 5
ruptured plaque

IVUS analysis



Patients and plaques profile

Informed consent obtained from 71 patients

Enrolled: 57 subjects

Dropouts during observation : 14

0-28 weeks : 39 subjects

Dropouts : 10 subjects

Dropouts (including due to different study terms): 14
Subjects excluded from efficacy evaluation : 5 (including one dropout)

0-28-80 weeks :
29 subjects

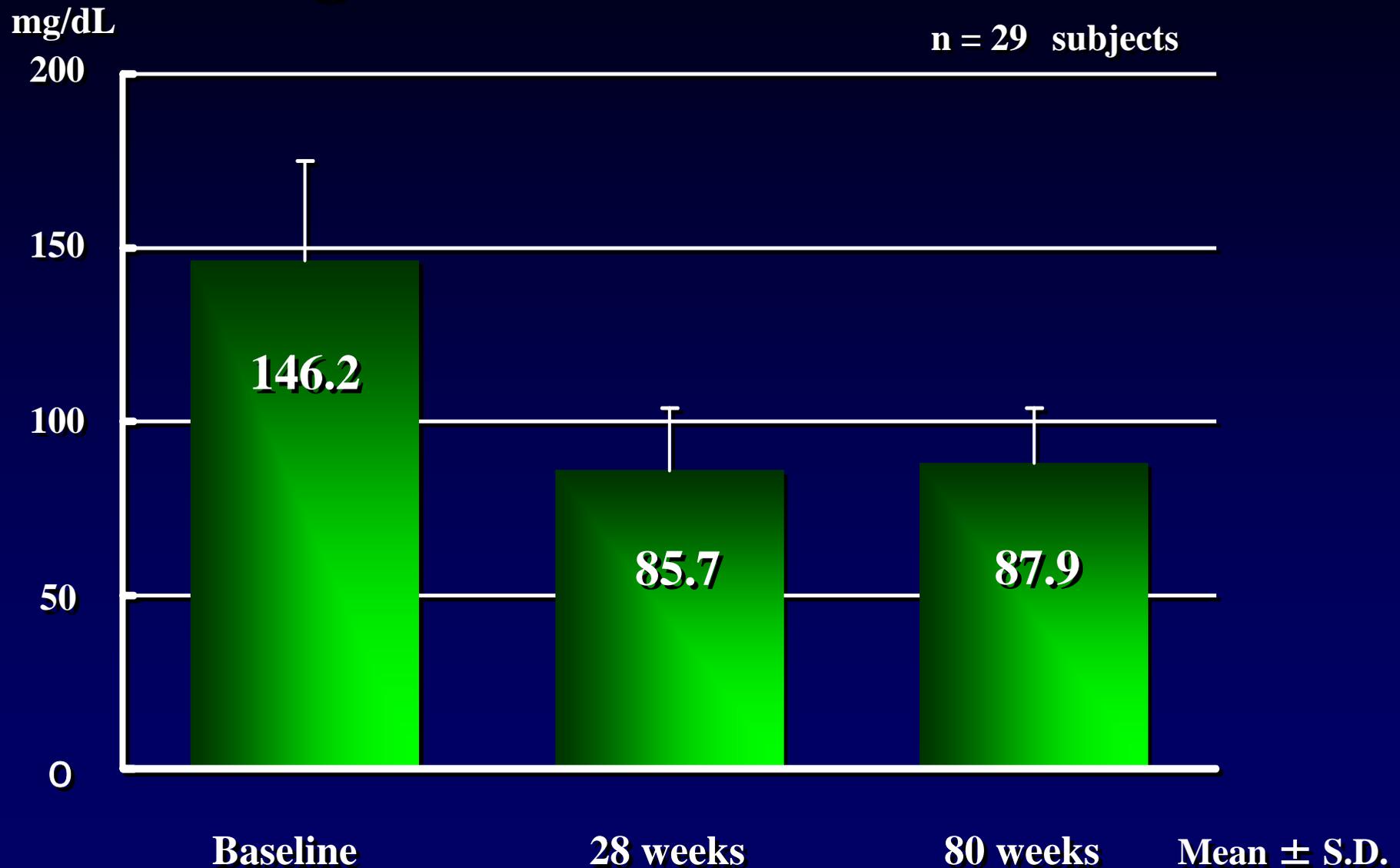
10 mg continued : 17 subjects
20 mg incremented : 12 subjects

Plaque number	0-28-80 weeks
Angioscopy	162
IVUS (volume)	57

Patients' characteristics (n=29)

Age,mean(SD)	59.0 (8.0)
Sex,n,(%)	
Male	24 (82.8)
Female	5 (17.2)
Angina,n,(%)	11 (37.9)
Previous myocardial infarction,n,(%)	19 (65.5)
Asymptomatic myocardial ischemia,(%)	2 (6.9)
Diabetes mellitus,n,(%)	9 (31.0)
BMI (SD)	24.4 (3.3)

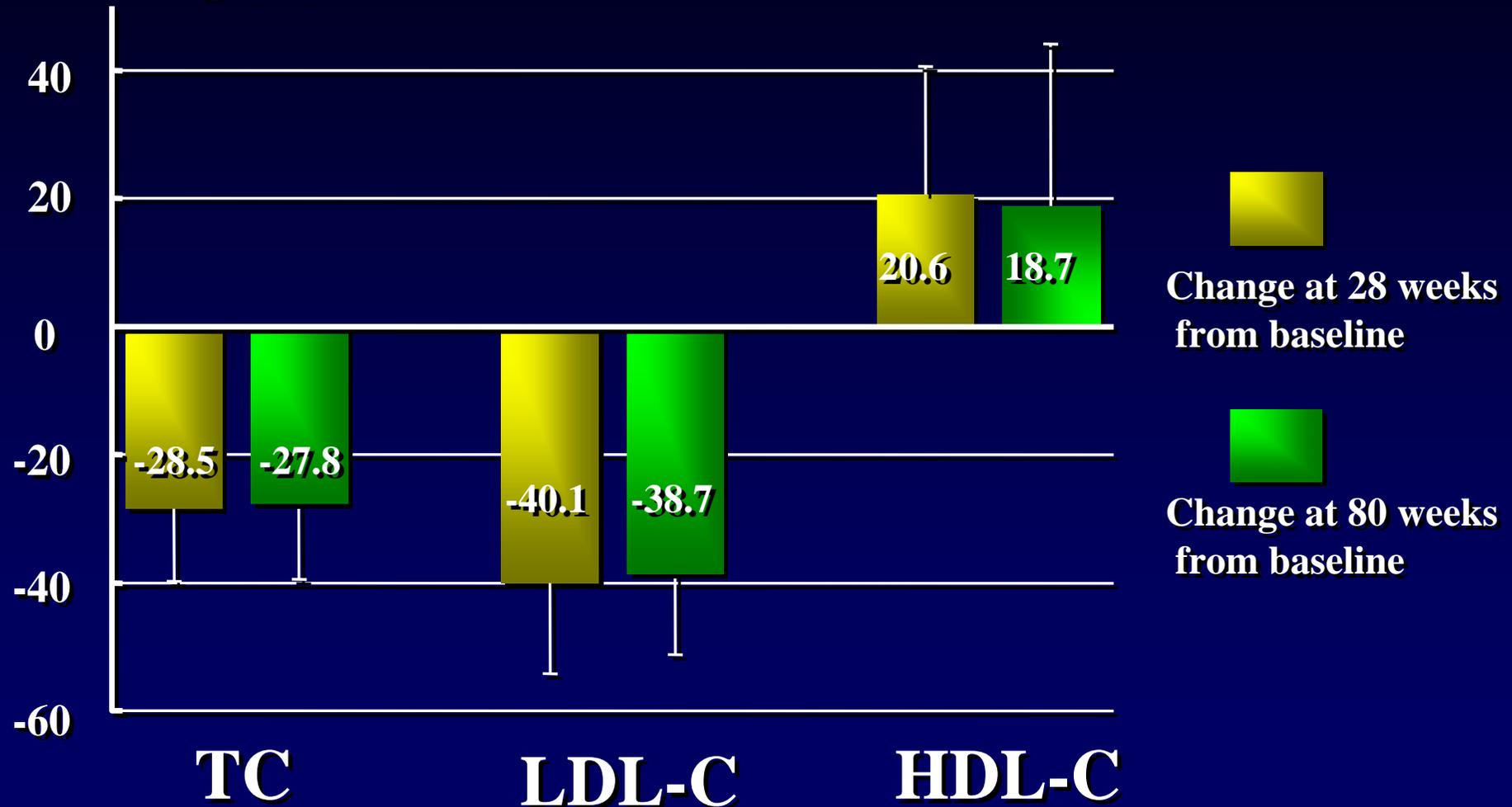
Changes in LDL-cholesterol



%Changes in lipid profile

Rate of change (%)

n = 29 subjects



Mean \pm S.D.

Case (angioscopy)

Grade 1

LDL-C 30% ↓

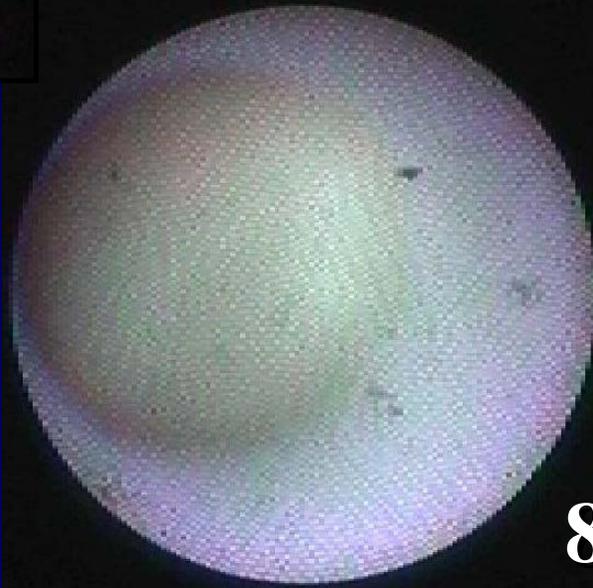
Grade 3



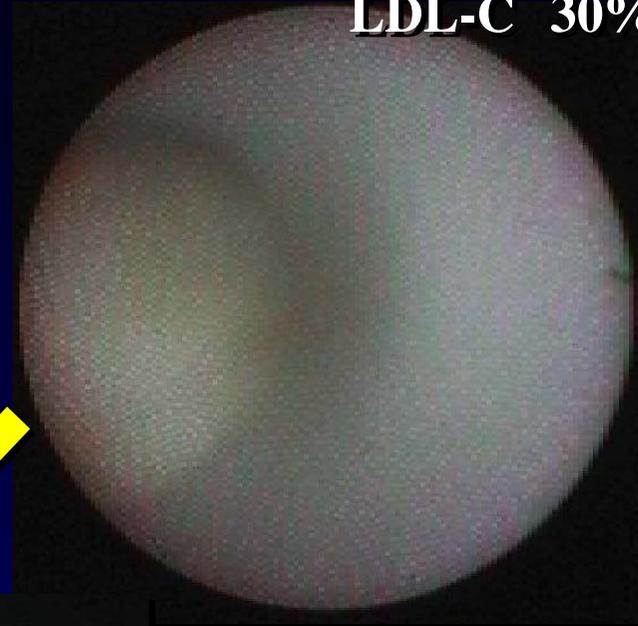
Baseline

Grade 1

LDL-C 21% ↓



80 weeks

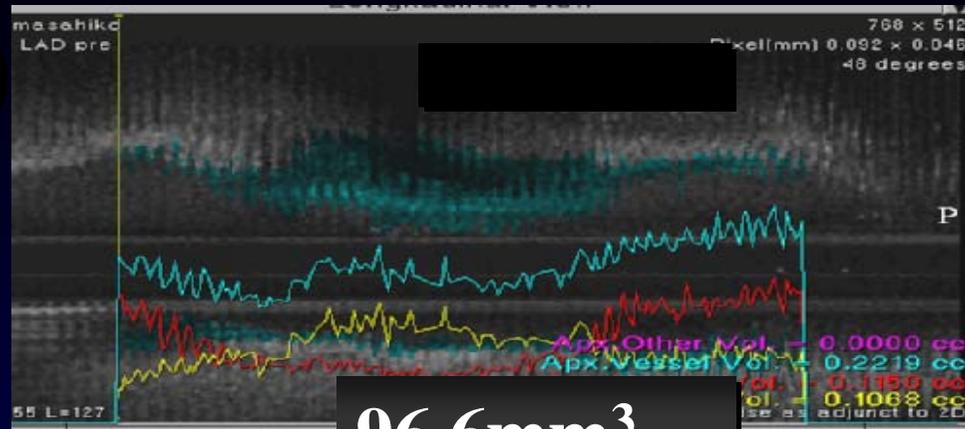


28 weeks



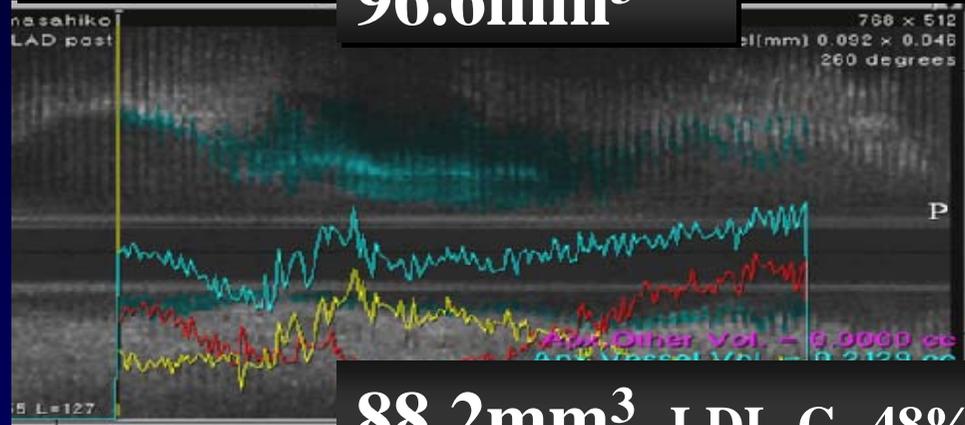
Case (IVUS)

Baseline



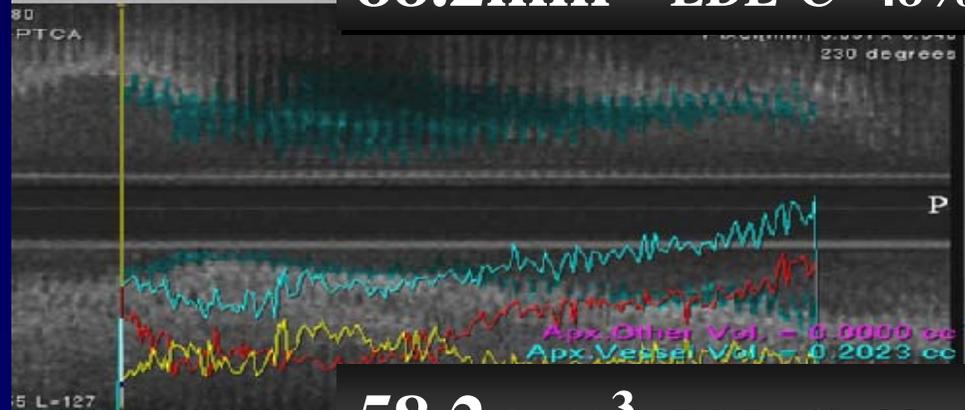
96.6mm³

28 weeks



88.2mm³ LDL-C 48% ↓

80 weeks

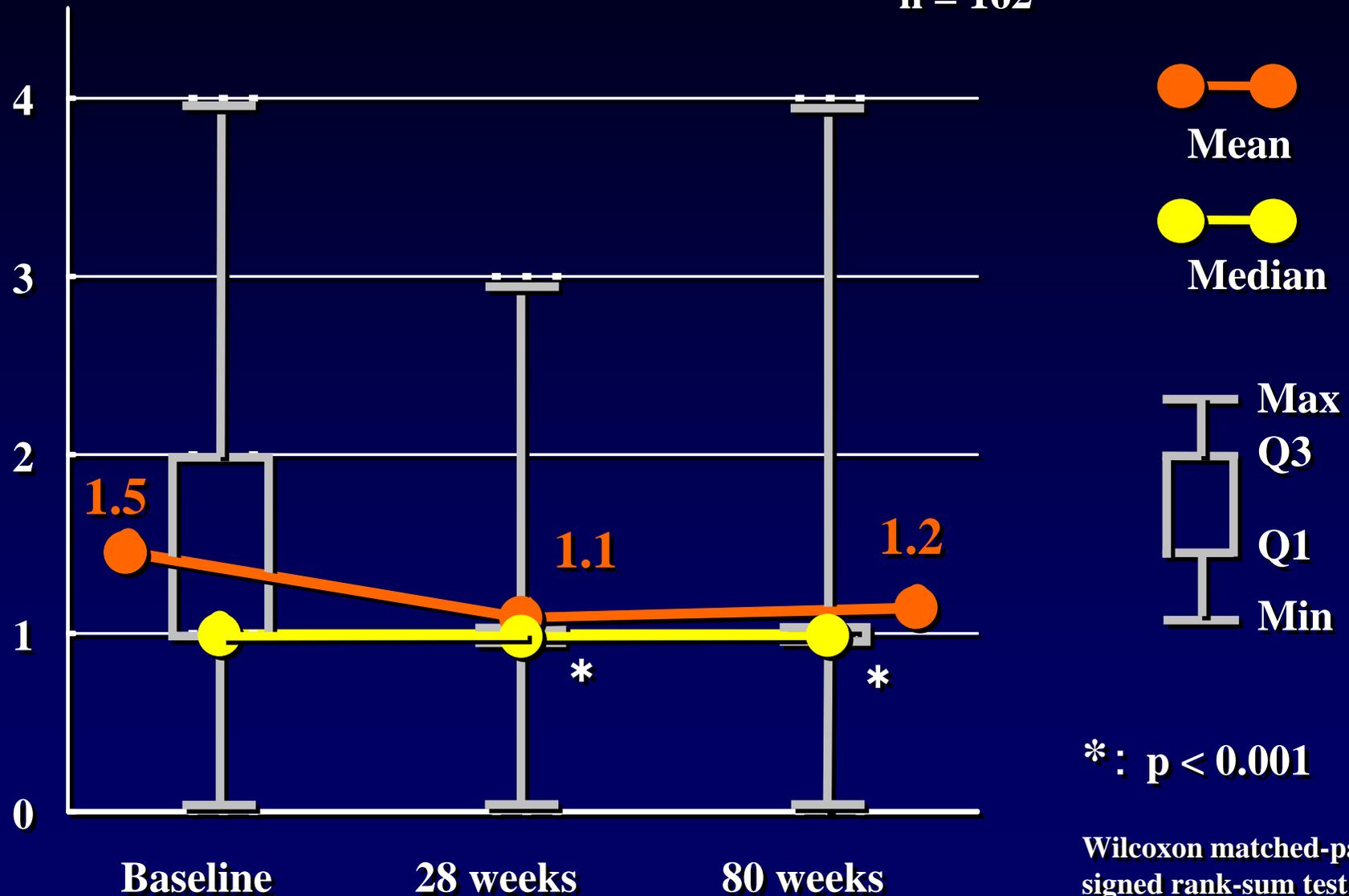


58.2mm³ LDL-C 38% ↓

Change in Angioscopic Grade

Grade

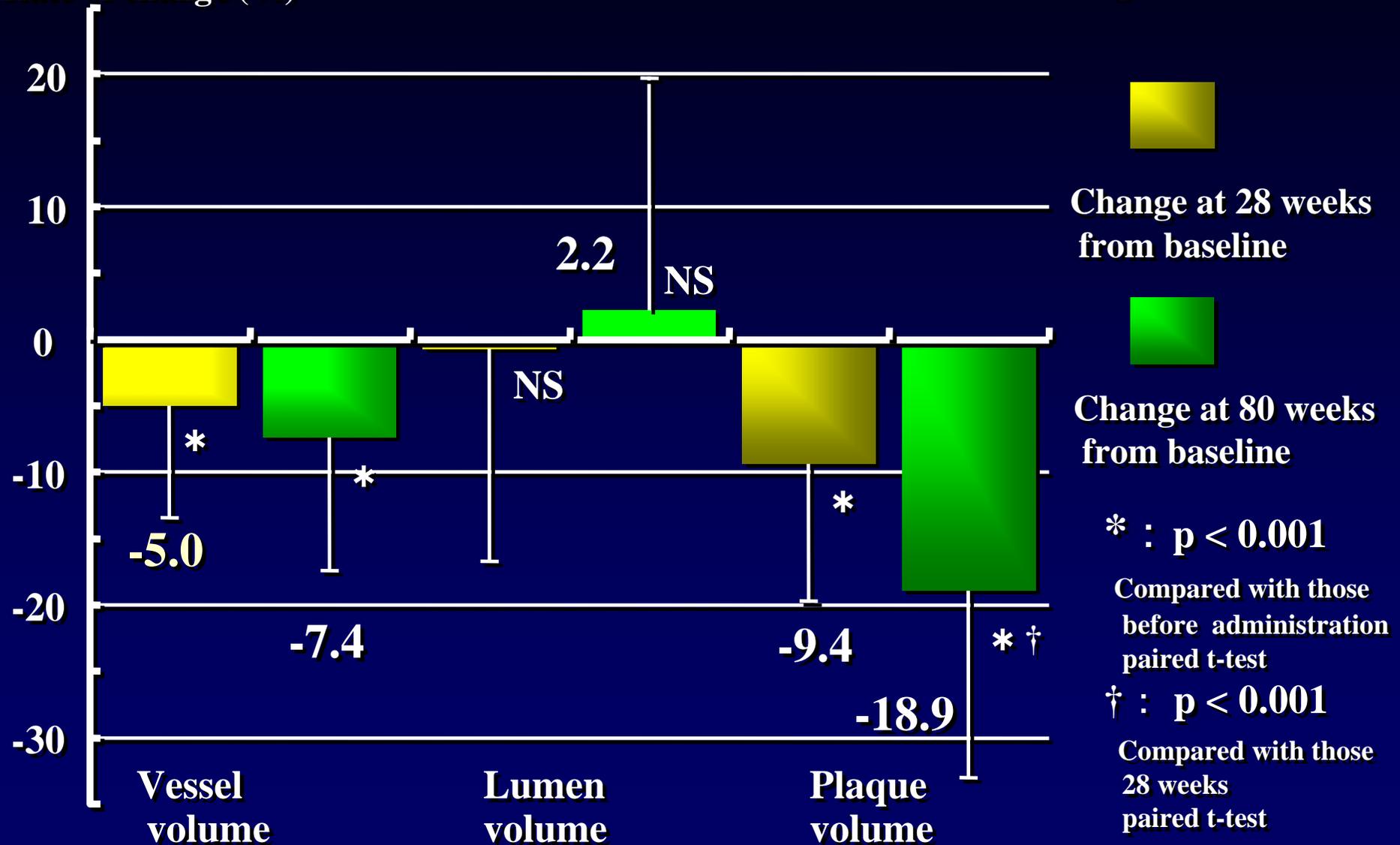
n = 162



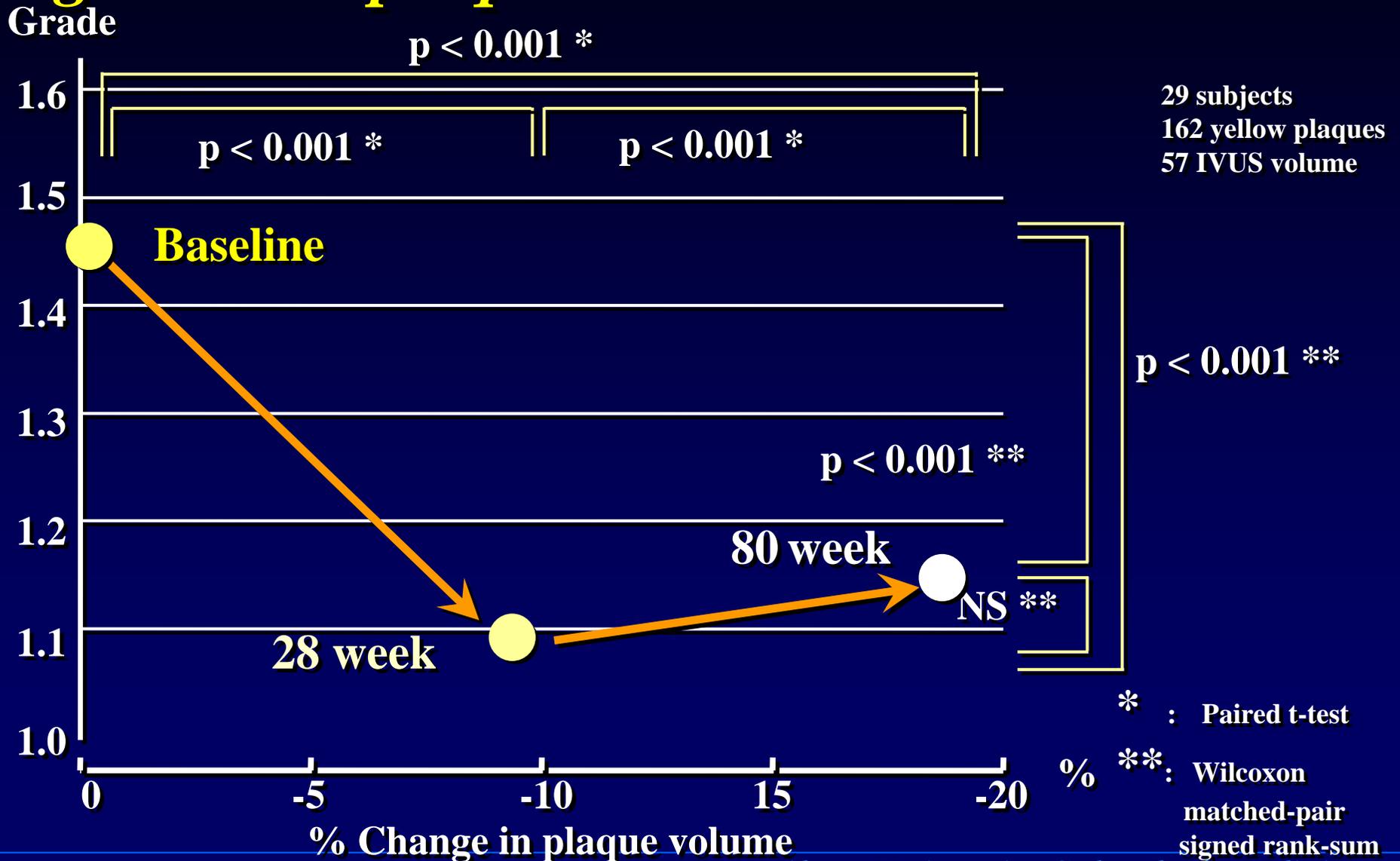
% Changes in IVUS parameters

n = 57 segments

Rate of change (%)



Changes in cross point of angioscopic grade and plaque volume



Summary

- ✓ **Lipid-lowering therapy with Atorvastatin achieved a significant reduction in color of yellow plaque up to 28 weeks and then remained up to 80 weeks.**
- ✓ **Lipid-lowering therapy with Atorvastatin increased regression of plaque volume with time at 28 weeks and 80 weeks.**
- ✓ **Reduction of yellow color intensity of plaque suggesting vascular endothelium stabilization and plaque regression proceeded along different time courses.**

Clinical Implication

In a patient with coronary artery disease, lipid-lowering therapy with Atorvastatin initiated in early phase and continued for a long time is necessary for continuous stabilization of the plaque.

Conclusion

Both stabilization and regression of the coronary plaque by the lipid lowering treatment with Atorvastatin results in the reduction of cardiac event.