

# **Investigation of Lipid Level Management Using Coronary Ultrasound to Assess Reduction of Atherosclerosis by CETP Inhibition and HDL Elevation**

**ILLUSTRATE**

**Presented at the American College of  
Cardiology Annual Scientific Session  
March, 2007**

**Presented by Dr. Steven E. Nissen**

# ILLUSTRATE Trial: Background

- The goal of the trial was to evaluate the effect of treatment with torcetrapib, a cholesteryl ester transfer protein (CETP) inhibitor, in addition to atorvastatin as compared with atorvastatin treatment alone on disease progression among patients with coronary artery disease.

# ILLUSTRATE Trial: Study Design

1188 patients, aged 18-75 years, with clinically indicated cardiac catheterization showing  $\geq 1$  stenosis on angiography with  $\geq 20\%$  narrowing and if target vessel had less than 50% obstruction throughout a segment  $\geq 40$ mm.

Randomized. Double-blind.  
Mean age = 57 years. 30% Female

R

4-10 week run-in phase of atorvastatin treatment titrated to achieve LDL level of 85-115mg/dl

**Atorvastatin + Torcetrapib**

60 mg  
n=591

**Atorvastatin + Placebo**

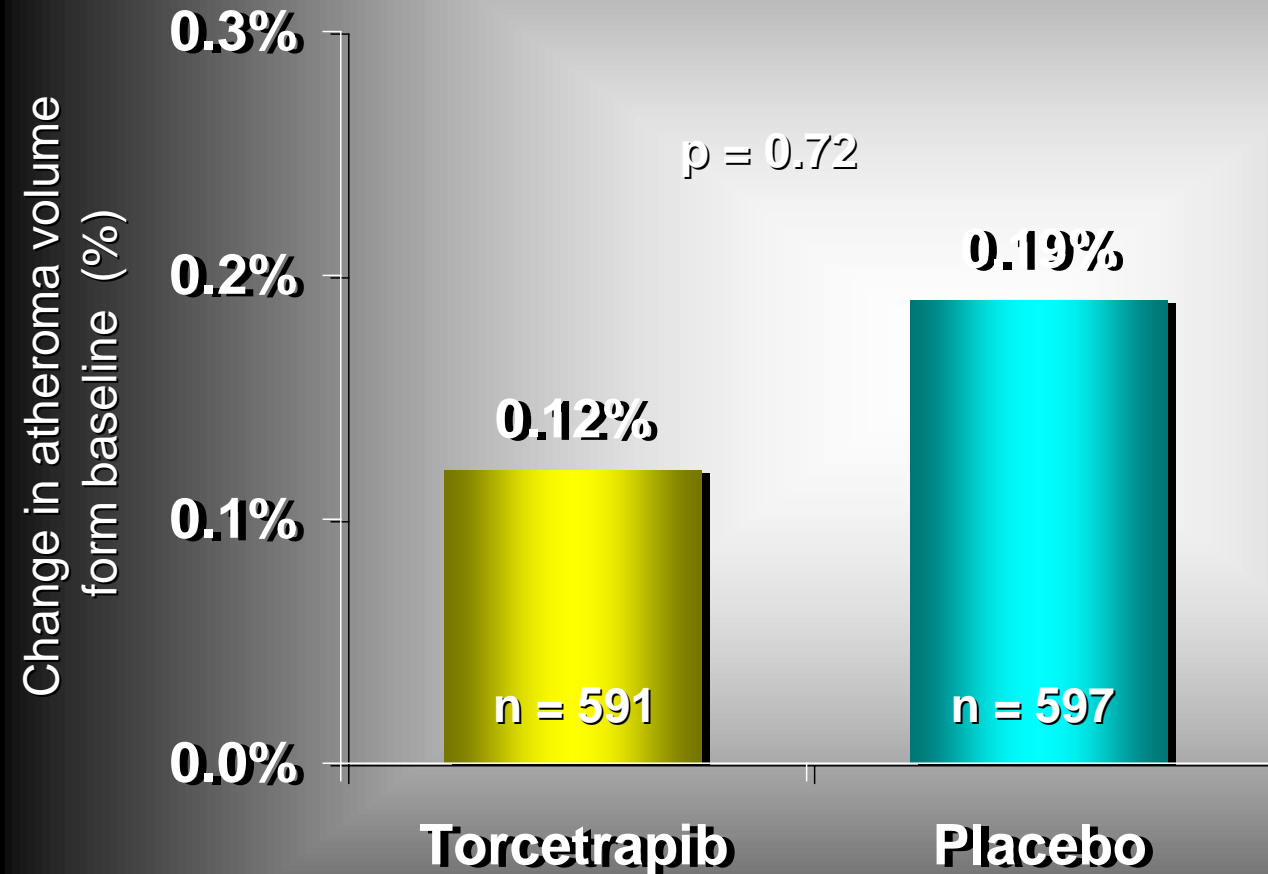
60 mg  
n=597

24 mos. follow up

- Primary Endpoint: Change in percent atheroma volume
- Secondary Endpoint: Normalized total atheroma volume; change in atheroma volume in the most diseased 10-mm segment

# ILLUSTRATE Trial: Primary Endpoint

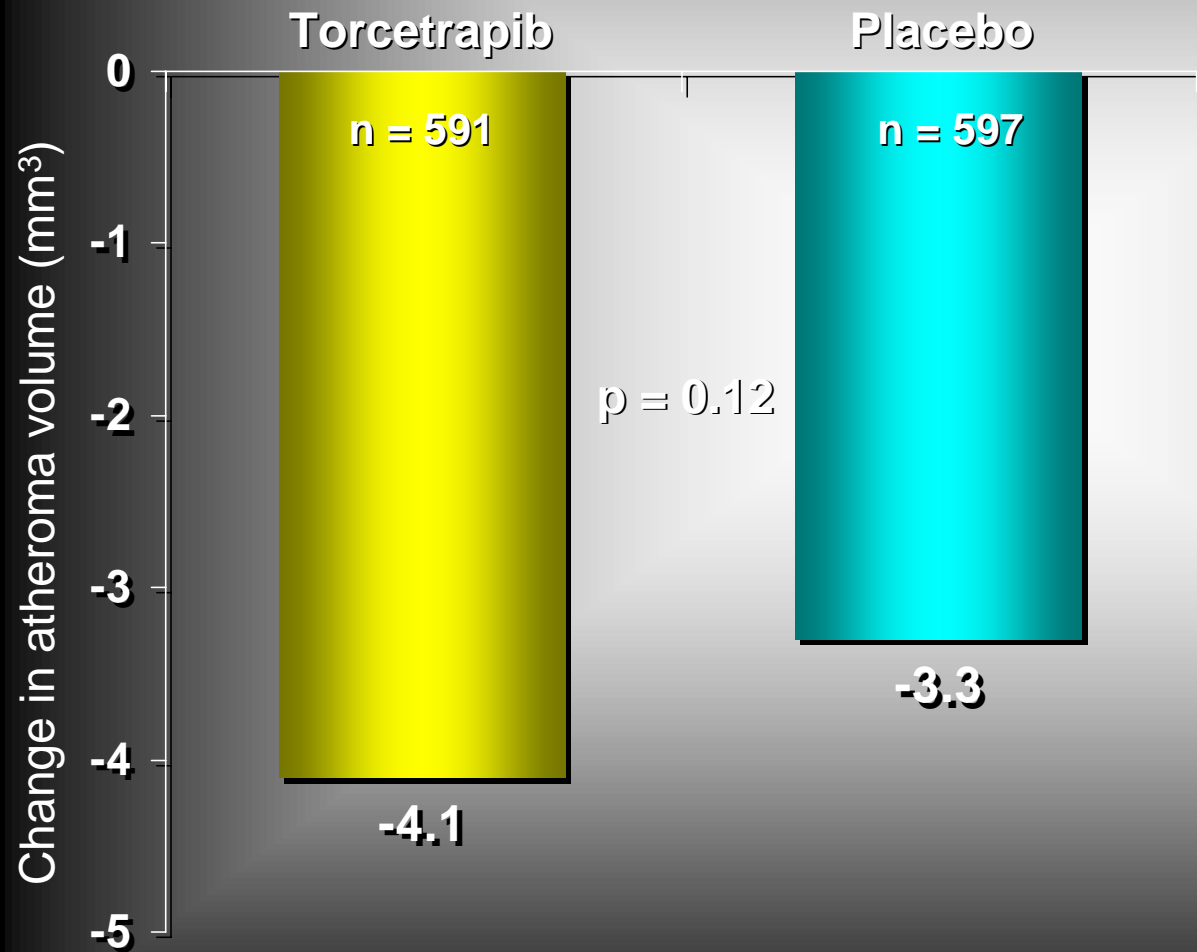
Percent change in atheroma volume from baseline



- The percent change in atheroma volume did not differ between treatment groups.

# ILLUSTRATE Trial: Secondary Endpoint

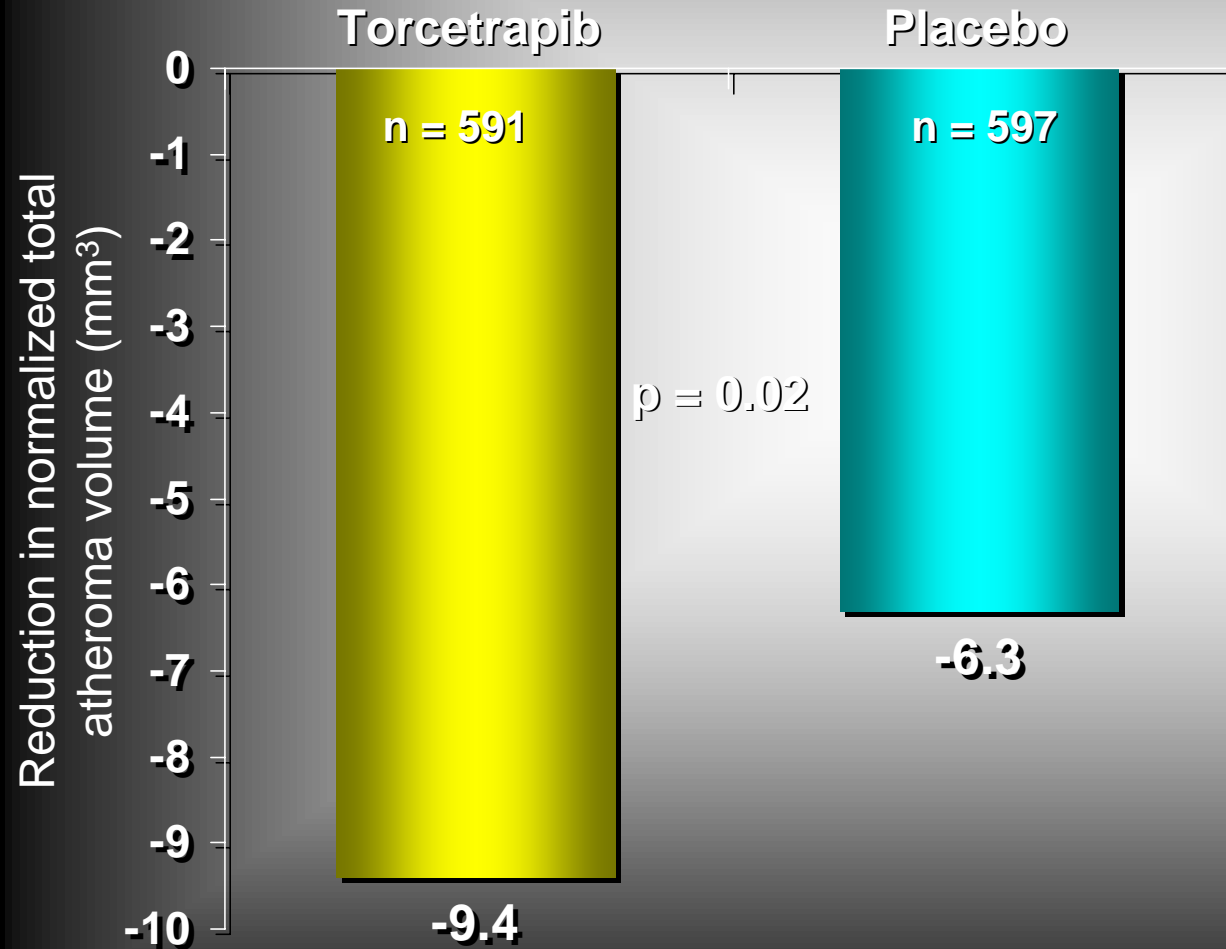
Change in atheroma volume of the most diseased 10mm segment



- The change in atheroma volume of the most diseased 10mm segment did not differ between the two treatment groups.

# ILLUSTRATE Trial: Secondary Endpoint

Reduction in normalized total atheroma volume



- The reduction in normalized total atheroma volume was greater in the torcetrapib group (-9.4 mm<sup>3</sup>) compared with atorvastatin alone (-6.3 mm<sup>3</sup>) (p=0.02).

# ILLUSTRATE Trial: Limitations

- Commercial development of torcetrapib was recently stopped after a large trial showed an increase in mortality with torcetrapib, along with an increase in blood pressure.
- The present trial, while much smaller than the other trial, did not show a difference in mortality with torcetrapib, but there were only 14 deaths.

# ILLUSTRATE Trial: Summary

- Among patients with coronary disease, treatment with the CETP inhibitor torcetrapib in addition to atorvastatin therapy was not associated with a difference in change in percent atheroma volume compared with atorvastatin alone at 24 months follow-up.

# ILLUSTRATE Trial: Summary Cont.

- Torcetrapib was effective in raising HDL in the present study.
- However, there was no effect on atherosclerosis progression, despite having the expected impact on increasing HDL and lowering LDL.