before treatment (78% vs 52%; p=0.007). Carl Tomasso, MD, Evanstown Northwestern Healthcare, Skokie, IL, suggested that PCI is indicated for patients who have a large amount of jeopardized myocardium or if OMT alone does not provide adequate relief of angina or the desired level of physical activity. He also emphasized that COURAGE did show several benefits of PCI: it led to a lower rate of subsequent revascularization, to better relief of angina over 1-3 years, and to better quality of life over 1-2 years.

Bernard J. Gersh, Mayo Clinic, Rochester, MN, commented that the COURAGE substudy results also suggest that the ACC/AHA guidelines for chronic stable angina are applicable to patients with silent ischemia. For patients with silent ischemia without overt angina or anginal equivalents, high-risk features on stress testing should be used as indications for angiography, said Dr. Gersh, and revascularization should be performed if "compelling" anatomy is identified.

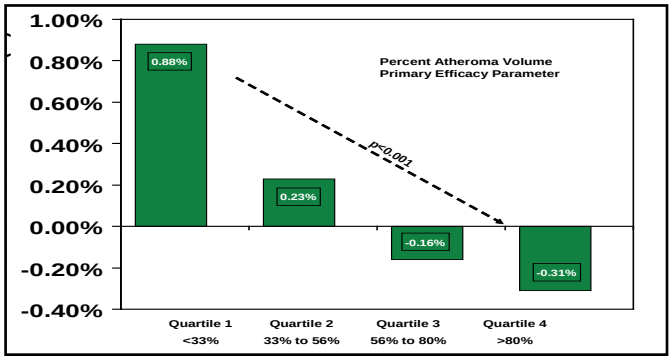
American College of Cardiology/ European Society of Cardiology Joint Symposium on Lipids

When the results of the ILLUSTRATE (Investigation of Lipid Level Management Using Coronary Ultrasound to Assess Reduction of Atherosclerosis by CETP Inhibition and HDL Elevation) trial [Nissen SJ et al. *N Engl J Med* 2007] called into question the efficacy of the cholesteryl ester transfer protein (CETP) inhibitor torcetrapib, many thought it signaled the end of the pursuit of these compounds for the treatment of dyslipidemia. Steven E. Nissen, MD, Cleveland Clinic, OH, discussed new data from ILLUSTRATE, which provide hope for the future of CETP inhibitors.

Although ILLUSTRATE showed that the CETP inhibitor torcetrapib increased HDL-C levels, the primary analysis did not show an effect on atherosclerotic progression. A new secondary analysis of the ILLUSTRATE data has shown that when percentages of HDL-C elevation are viewed as incremental quartiles, there is a progressive decrease in rate of progression of coronary atherosclerosis relative to the extent of HDL-C elevation. Patients who reached the highest HDL-C level (>86 mg/dL) actually achieved atherosclerosis regression (Figure 1).

Several new CETP inhibitors are entering clinical trials, and Dr. Nissen expressed hope that the newer drugs might prove to be clinically useful, because they do not appear to cause an increase in blood pressure, as was shown with torcetrapib.

Figure 1. Torcetrapib Results: Quartiles of HDL-C Elevation.



Johan W. Jukema, MD, Leiden University Medical Center, Amsterdam, The Netherlands, spoke about statin therapy in three subgroups of patients who are known to be at risk for cardiovascular (CV) events: patients with chronic kidney disease, older patients with moderate to severe ischemic systolic heart failure, and the at-risk elderly.

According to Prof. Jukema, study results are mixed for the first two groups. For patients with chronic kidney disease, he cited results from a meta-analysis that showed that the use of statins can significantly reduce lipid concentrations (total cholesterol -42.28 [95% CI, -47.25 to -37.32]; LDL-C -43.12 [95% CI, -47.85 to -38.40]; HDL-C +0.41 [95% CI, -0.78 to 1.60]; and triglycerides -23.71 [95% CI, -33.52 to -13.90]), as well as mortality (RR 0.81; 95% CI, 0.73 to 0.90), but that they provide no benefit for all-cause mortality (RR 0.92, 95% CI, 0.82 to 1.03) [Strippoli GFM et al. *Br Med J* 2008].

For older patients with ischemic systolic heart failure, Prof. Jukema cited new data from CORONA (Controlled Rosuvastatin Multinational Trial in Heart Failure), which showed that although the use of rosuvastatin 10 mg daily significantly decreased the number of related hospitalizations (2564 vs 2193, placebo vs rosuvastatin, respectively; p<0.001), there was no effect on the primary composite endpoint of death, non-fatal MI, or non-fatal stroke (HR 0.92; 95% CI, 0.83 to 1.02; p=0.12) [Kjekshus J et al. *N Engl J Med* 2007]. These findings were surprising because prior retrospective analyses with atorvastatin 80 mg [Scirica BM et al. *J Am Col Cardiol* 2006; Khush KK et al. *Circulation* 2007] had suggested that such patients might benefit from high-dose statin therapy.

Prof. Jukema also discussed the results of a meta-analysis that examined the effect of statin therapy for secondary prevention in elderly patients with coronary heart disease, which showed that not only do statins reduce all-cause mortality in these patients (15.6% with statins vs 18.7% with placebo, RR reduction 22% over 5 years; 95% CI, 0.65 to 0.89),

but the extent of the effect is much larger than originally thought [Afilalo J et al. *J Am Col Cardiol* 2008; Table 1].

Table 1. Effect of Statin Therapy for Secondary Prevention in the Elderly.

Outcome	Percent Reduction	HR (95% CI)
Coronary heart disease	30%	0.70 (0.53 – 0.83)
Non-fatal myocardial infarction	26%	0.74 (0.60 – 0.89)
Revascularization	30%	0.70 (0.53 – 0.83)
Stroke	25%	0.75 (0.56 – 0.94)

Robert S. Rosenson, MD, University of Michigan, Ann Arbor, MI, reviewed several studies that evaluated the relationship between obesity and mortality, noting that while obese individuals (BMI 30-35) may not have an increased risk for mortality (RR 0.97; 95% CI, 0.82-1.15), the risk is increased for the severely (BMI >35) obese (RR 1.88; 95% CI, 1.05–3.34) [Romero-Corral A et al. *Lancet* 2006].

Investigators who evaluated the differences in risk among obese and severely obese individuals have suggested that insulin sensitivity may be a better predictor than obesity alone in predicting risk (Table 2; McLaughlin T et al. *Arch Int Med* 2007; Reaven G. *Diab Vasc Dis Res* 2005).

Table 2. CV and Diabetes Risk Factors in Obese Individuals Based on Tertile of SSPG Concentration.

Risk Factors	Tertile 1 (n=70)	Tertile 2 (n=70)	Tertile 3 (n=71)	p Value†	p Value For Trend‡
Systolic BP, mm Hg	123(18)	130 (17)	139 (20)	<.001	<.001
Diastolic BP, mm Hg	75 (10)	78 (12)	83 (3)	<.001	<.001
TG level, mg/dL	114 (51)	156 (66)	198 (105)	<.001	<.001
HDL-C level, mg/dL	50(13)	47 (13)	41 (9)	<.001	<.001
LDL-C level, mg/dL	123 (38)	134 (33)	123 (29)	.88	.77
Fasting plasma glucose level, mg/dL	95 (11)	99 (10)	103 (11)	<.001	<.001
2-h Plasma glucose level during OGTT, mg/dL	104 (19)	124 (35)	139 (39)	<.001	<.001
IFG level, No. (%) of participants	20 (29)	32 (46)	48 (68)	<.001	<.001
IGT, No. (%) of participants	1 (1)	20 (29)	33 (46)	<.001	<.001

Abbreviations: BP, blood pressure; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; SSPG, steady-state plasma glucose; TG, triglyceride.
†Calculated as analysis of covariance, adjusted for age, body mass index, and sex.
‡Analyzed via general linear model for continuous variables and Cochran-Armitage test for categorical variables.

Dr. Rosenson noted that cardiovascular risk is heterogeneous among obese individuals and that more emphasis should be placed on identifying individuals at risk for cardiovascular disease based on their level of insulin resistance versus obesity alone.

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The controversy over the results of the ENHANCE trial will likely remain until the results of the IMPROVE-IT trial are available in 2012. In the meantime, the American Heart Association and the American College of Cardiology have issued the following joint statement on ENHANCE:

> *'The study reinforces the need to adhere to current American College of Cardiology/ American Heart Association Guidelines which recommend statins to the maximally tolerated dose or to goal as first line treatment for patients with coronary artery disease. The data from the ENHANCE study should be considered as the NHLBI guidelines writing group is working on their update of the national cholesterol treatment guidelines in the coming months.'*

Full text of the statement is available at:http://americanheart.mediaroom.com/index.php?s=43&item=386

Additional reading:

1. Brown BG, et al. Does ENHANCE Diminish Confidence in Lowering LDL or in Ezetimibe? *N Engl J Med* 2008;358:1504-07.
2. Drazen JM, et al Cholesterol Lowering and Ezetimibe. *N Engl J Med* 2008;358:1507-08.
3. Jackevicius CA, et al. Use of Ezetimibe in the United States and Canada. *N Engl J Med* 2008:358 (www.nejm.org on March 30, 2008 (10.1056/NEJMsa0801461). Special Article.
4. Kastelein JJP, et al. Simvastatin with or without Ezetimibe in Familial Hypercholesterolemia. 2008 *N Engl J Med*;358:1431-1443.

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Despite the highly significant correlation between AV block and death, differentiating between all-cause cardiac death and sudden cardiac death secondary to ventricular arrhythmias is difficult, Dr. Thomsen said. To investigate this issue, CARISMA investigators are performing additional analyses to further explore the relationship between baseline left bundle branch block and subsequent risk of fatal ventricular arrhythmias and AV block.

In summary, findings from the CARISMA observational study suggest that an implantable ECG loop recorder—typically used to identify the cause of syncope—may help clinicians risk-stratify patients with reduced LV function following acute MI.