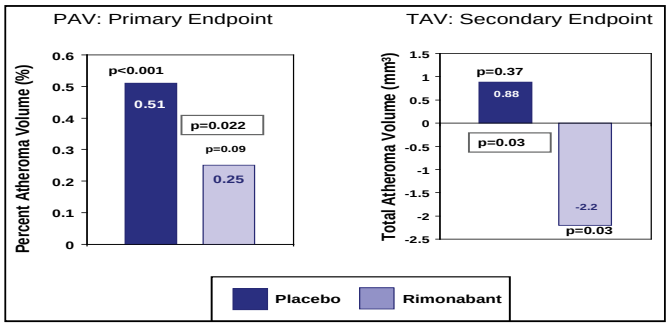
the United States but is available in some European countries. The percent atheroma volume (PAV) and normalized total atheroma volume (TAV) on IVUS were determined in all patients at the beginning of the study and again at 18 months in the 676 patients who completed the trial, regardless of whether they were still taking the study drug.

Steven E. Nissen, MD, Cleveland Clinic, Cleveland, OH, reported that rimonabant (compared with placebo) failed to reduce the primary endpoint of PAV (+0.25% change from baseline with rimonabant vs +0.51% with placebo; p=0.22; Figure 1). However, there was a significant difference between the two groups with respect to the secondary endpoint of change in TAV from baseline (-2.2 mm^3 rimonabant vs +0.88 mm^3 placebo; p=0.03).

Figure 1. Primary and Secondary IVUS Endpoints.



Of concern in the study was the higher frequency of psychiatric adverse events in the rimonabant arm (43.4% vs 28.4%; p<0.001). This difference was primarily driven by significant increases in anxiety (18.0% vs 11.8%; p=0.01) and depression (16.8% vs 11.3%; p=0.02). Dr. Nissen pointed out that approximately one-quarter of the patients in the study had a history of psychiatric disease at the start of the trial. The risk of psychiatric adverse events was a factor in the unanimous recommendation against approval of the drug by a U.S. Food and Drug Administration advisory panel in 2007.

The lipid-lowering benefits of both rosuvastatin and rimonabant were confirmed by these two studies. Rosuvastatin reduced low-density lipoprotein (LDL) levels by more than 50% and increased high-density lipoprotein (HDL) levels by 14%, while rimonabant increased HDL by 22% and reduced triglyceride levels by 21%. Dr. Ballantyne noted that it may be necessary to reduce LDL by >50% or set a target LDL near 60 mg/dL to induce plaque regression in coronary atherosclerosis.

The results of the QCA analysis from the ASTEROID trial were published online (*Circulation* 2008), and the primary results of STRADIVARIUS were published in *JAMA* 2008;299:1547-1560.

Cardiac Arrhythmias and Risk Stratification after MI

Patients who survive an acute myocardial infarction (MI) with diminished left ventricular (LV) function experience frequent and treatable arrhythmias, according to findings from the Cardiac Arrhythmias and Risk Stratification after Myocardial Infarction (CARISMA) observational study. Moreover, high-degree atrioventricular (AV) block appears to independently predict cardiac death in the post-MI patient population.

"The insertable ECG loop recorder is a diagnostic tool that should be considered to guide medical and device therapy in patients who survive myocardial infarction," said Poul Erik Bloch Thomsen, MD, Gentofte University Hospital, Copenhagen, Denmark, principal investigator of the CARISMA trial.

CARISMA is the first long-term observational study to examine implantable loop recorder data among post-MI patients. The study was designed to determine the risk of tachyarrhythmia and sudden death in patients who do not meet the criteria for an implantable cardioverter defibrillator (ICD) despite mild to moderate structural damage following an acute MI.

In CARISMA, investigators implanted insertable loop recorders in 297 patients an average of 11 days after MI. All patients had a low ejection fraction (EF<40%), and none had an ICD. During a 2-year follow-up, the loop recorders provided information every 4 months on the incidence of any arrhythmias: sinus bradycardia, sinus arrest, atrial fibrillation (AF), second or third degree AV block, ventricular tachycardia (VT), and fibrillation.

After a mean follow-up of 1.9 years, 137 patients (46%) had evidence of at least one of the pre-specified arrhythmias, of which only 14% was symptomatic.

New AF (≥125 bpm), the most frequent arrhythmia, was documented in 27% of patients. Sinus bradycardia (<30 bpm), AV block (<30 bpm), non-sustained VT (≥125 bpm, ≥16 beats), and sustained VT (≥125 bpm, ≥30 seconds) were each observed in approximately 17% of patients.

In a univariate analysis, AV block (HR 7.0; p=0.0004), sinus bradycardia (HR 5.8; p=0.004), and non-sustained VT (HR 3.4; p=0.025) appeared to predict cardiac death. However, by multivariate analysis, high-degree AV block remained the only independent predictor of cardiac death (HR 4.8; p<0.001).

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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.