New clinical data shows that intensive cholesterol-lowering to targets below currently recommended levels significantly reduces the risk of myocardial infarction (MI) and stroke in patients with diabetes and stable coronary heart disease (CHD).

James Shepherd, M.D., of Glasgow, UK, presented the diabetic portion of the Treating to New Targets (TNT) study at the American Diabetes Association 65th Annual Meeting and Scientific Sessions. The main trial was first presented during the American College of Cardiology Scientific Sessions earlier this year, by John LaRosa, M.D., State University of New York Downstate Medical Center, Brooklyn, and subsequently published in The New England Journal of Medicine.

TNT was the first large randomized clinical trial to compare 80 mg and 10 mg atorvastatin (Lipitor, Pfizer) as secondary prevention in patients with stable CHD. Eligible patients were aged 35 to 75 years and had clinical evidence of CHD. After a washout period of 1 to 8 weeks, 15,464 patients were entered an open-label run-in phase with 10 mg atorvastatin.

**CONTROL LDL CHOLESTEROL**

To be eligible for enrollment, patients had to have their LDL cholesterol ≤130 mg/dL at the end of the run-in phase. A total of 10,001 patients reached this level and were then randomized to treatment with either 10 mg or 80 mg of atorvastatin daily. Mean follow-up was 4.9 years.

Over the course of the trial, investigators looked for a risk reduction in composite vascular phenomenon of coronary death, nonfatal MI, fatal and nonfatal stroke and resuscitative cardiac arrest, according to Dr. Shepherd. Risk reduction was the primary endpoint of the study.

To assess the benefit of treatment to different LDL levels, the target was <100 mg/dL in the atorvastatin 10-mg group and 75 mg/dL in the atorvastatin 80-mg group. Total cholesterol and triglycerides decreased significantly in the atorvastatin 80-mg group, and nonsignificant increases in HDL were seen in both groups.

In the main portion of the TNT study, high-dose atorvastatin decreased first major cardiovascular events by 22% compared to the lower dose (8.7% vs 10.9%; P <.001). Nonfatal MI was also decreased by 22% (4.9% vs 6.2%; P =0.004), and fatal or nonfatal stroke was reduced by 25% (2.3% vs 3.1%; P =0.02). A trend toward a decrease in coronary mortality was observed with atorvastatin 80 mg (2.0% vs 2.5%; HR, 0.80; P =.09).

**WHAT ABOUT DIABETICS IN TNT?**

Diabetes is a coronary risk equivalent, Dr. Shepherd said. “The recent ATP III guidelines have been changed to include the fact that diabetic patients should be treated for their vascular risk as if they had existing coronary disease,” he said.

There were 1,500 diabetic patients in TNT, which is roughly 15% of the total cohort. Half were randomized...
There are numerous benefits to lowering LDL cholesterol. However, LDL levels between 100 and 130 mg/dl may still cause myocardial infarction and other coronary events in a substantial number of patients. John C. LaRosa, M.D., president, SUNY Downstate Medical Center, and colleagues enrolled patients in the Treating To New Targets (TNT) study to determine if lowering the current guideline in patients with stable coronary heart disease was as safe and effective as in patients with acute coronary syndromes. Dr. LaRosa is chairman of the TNT steering committee.

According to a news release from the American College of Cardiology, optimal treatment targets for patients with coronary heart disease (CHD) are still the subject of substantial debate. In March, Dr. LaRosa first presented this study at the 54th Annual Scientific Sessions in Orlando. One major goal of the study was to decrease LDL levels to 75 mg/dL in the enrolled patients.

“Is it useful to get LDL cholesterol levels down so low? And secondly, is it safe? These are landmark questions,” Dr. LaRosa said in the news release.

The study was also published in The New England Journal of Medicine. Investigators evaluated the patients for signs of a first major cardiovascular event. This was defined as either death from CHD, nonfatal myocardial infarction that was not caused by a hospital procedure, resuscitation after cardiac arrest or fatal or nonfatal stroke.

After 49 years follow-up, those patients who were given 10 mg atorvastatin had LDL levels of 101 mg/dL. However, patients who received 80 mg of atorvastatin decreased their LDL level to 77 mg/dL. Investigators concluded in The New England Journal of Medicine that if patients with stable coronary heart disease were treated with 80 mg of atorvastatin, a clinical benefit was seen in regards to substantial coronary events.