New Results Uphold High-Dose Statin for CHD

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DALLAS — Aggressive statin therapy is now the standard of care for patients with established coronary heart disease, even though the results from the most recent major test of a high-dose statin regimen failed to show a statistically significant benefit, compared with a lower-dose statin regimen, in almost 9,000 patients.

The 11% relative reduction in major coronary events (death, myocardial infarction, or cardiac arrest and resuscitation) seen in the Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) study, which compared an 80-mg/day regimen of atorvastatin against a 20-mg or 40-mg/day regimen of simvastatin, was "consistent with the results of other statin trials, such as PROVE-IT and TNT," Dr. Terje R. Pedersen said at the annual scientific sessions of the American Heart Association.

"There is no doubt that lower levels of low-density lipoprotein cholesterol are better," said Dr. Pedersen, a professor of medicine and director of the Center for Preventive Medicine at Ullevål University Hospital, Oslo. He was the lead investigator for the IDEAL study, which was published concurrently with his report at the meeting (JAMA 2005;294:2437-45).

The results of both IDEAL and TNT (Treating to New Targets) "strengthened the case for incremental benefits from lowering LDL cholesterol well below 100 mg/dL," commented Dr. Scott Grundy, director of the Center for Human Nutrition at the University of Texas Southwestern Medical Center in Dallas. Regimens that produce very low levels of LDL cholesterol "will be increasingly accepted as the standard treatment for secondary prevention."

"Results from a single trial are sometimes hard to interpret. The results from IDEAL, TNT, PROVE-IT [Pravastatin or Atorvastatin Evaluation and Infection Therapy], REVERSAL [Reversal of Atherosclerosis With Aggressive Lipid Lowering], and other trials may not always reach statistical significance, but if you put them all together, people are moving toward more intensive statin treatment," commented Dr. Steven E. Nissen, medical director of the Cardiovascular Coordinating Center at the Cleveland Clinic. "You should try to get the LDL cholesterol as low as you can, safely. In both IDEAL and TNT, most patients did not get to 70 mg/dL or less, but even if only 25%-35% of patients get there, that's good."

IDEAL enrolled 8,888 patients aged 80 or younger who had a history of a definite myocardial infarction and who qualified for statin therapy based on national treatment guidelines at the time of enrollment. Patients were entered at 190 ambulatory cardiology and private specialist centers in Denmark, Finland, Iceland, the Netherlands, Norway, and Sweden from March 1999 to March 2001. Patients were randomized to treatment with either 20 mg/day simvastatin or 80 mg/day atorvastatin and followed for an average of 4.8 years.

After the first 24 weeks of treatment, 21% of patients in the simvastatin group had their dosage raised to 40 mg/day; by the end of the study, 23% of patients in the simvastatin group were receiving 40 mg/day, with the rest on 20 mg/day. By the end of the study, 13% of patients in the atorvastatin group had their dosage reduced to 40 mg/day.

The incidence of major coronary events was 10.4% in the simvastatin group and 9.3% in the atorvastatin group, an 11% relative risk reduction that fell slightly short of statistical significance. But Dr. Pedersen said that other secondary end points showed statistically significant differences in favor of the high-dose group, including a 13% relative reduction in major cardiovascular disease events and a 16% cut in any coronary heart disease event.

With safety data from almost 4,000 patients treated with 80 mg/day of atorvastatin for almost 5 years, the results also bolstered the apparent safety of aggressive lipid lowering. The results showed no difference between the two groups in all-cause mortality, and no difference between the two study groups in the incidence of serious adverse events. A small proportion of patients, less than 1.5%, had major liver enzyme elevations on the 80 mg/day regimen. Myopathy was diagnosed in 0.14% of patients on this regimen, and 0.05% had rhabdomyolysis.

The IDEAL study was sponsored by Pfizer Inc. Dr. Pedersen has been a consultant to and a speaker for Pfizer. ■