Was the AIM-HIGH Trial a Failure?

I thought it is extremely important to talk about the AIM-HIGH trial failure since it has dominated the news and disappointed many clinicians. I will first state some facts about the trial and then give some of my own thoughts.

The AIM-HIGH study analyzed whether raising HDL through the combination statin and niacin therapy would reduce the risk of having a heart attack in people with established heart disease. But the therapy showed no benefit and the study was brought to an abrupt halt more than a year before the anticipated end date.

On Thursday, May 26, 2011, the National Heart Lung and Blood Institute (NHLBI) formally ended the highly-anticipated AIM-HIGH trial earlier than expected due to futility. This large-scale outcomes study was designed to evaluate the impact of adding extended-release niacin to statin therapy (simvastatin) in patients with established coronary disease. The question this study was poised to answer was whether increasing HDL cholesterol and lowering triglycerides in patients with low HDL cholesterol and high triglycerides will reduce the risk of cardiovascular events in patients whose LDL cholesterol was already within a desirable range with statin therapy.

Clinicians have been using extended-release niacin to treat patients with low HDL-C since niacin has previously demonstrated benefit in earlier studies in conjunction with statins and other drugs. While niacin alone was shown to reduce myocardial infarction, stroke, and the need for coronary bypass surgery in a couple of very small previous studies, it should be recognized that no trials compared statin therapy to niacin plus statin therapy until the AIM-HIGH trial.

I think it is important to note that the current NCEP ATP III guidelines, which are going to be updated at the end of this year, has no goal of HDL cholesterol above "normal" that is ideal and that raising with medications is an optional tertiary goal of cholesterol management. Clinicians and patients need to know it's not about raising HDL cholesterol or lowering triglycerides. We already understand that low HDL cholesterol is a risk factor; however, there is no solid data to show that raising the HDL number does anything. We do not have a qualitative test to measure HDL function so we are stuck with a simple number that does not reflect functionality. In simple terms, there is no test to measure how well your HDL cholesterol works. If raising HDL-C was the answer, the prevalence of heart disease wouldn't double in the next century as projected. A good example of this is what the data showed in the Heart and Estrogen Replacement Study (HERS). In this study,20% of the women who had heart attacks had their HDL cholesterol between 60-80 mg/dl. This value is way above what is considered normal.

I believe that we need to refocus our evaluation and treatment of patients with cardiometabolic risk. The ADA/ACC 2008 Consensus Statement about lipoprotein testing in patients with cardiometabolic risk recommends advanced lipoprotein testing in patients with moderate to very high risk of cardiovascular morbidity and mortality. My belief is that the clinical focus should be on what's called, the "atherogenic lipoprotein particles" or LDL-P which penetrate the artery wall causing atherosclerosis. If this can be prevented then atherosclerosis doesn't occur. The most important diagnostic lipid blood test quantitates the number of atherogenic LDL and/or ApoB lipoprotein particles. Lipid specialists can then treat patients with appropriate medicines. Frankly, I'm somewhat happy that these results showed that Niaspan use alone, without a statin was not effective. Statins have been shown in numerous studies to be the "key" drug therapy in reducing heart related events. Too many physicians are just using Niaspan alone to treat the low HDL cholesterol. My hope is that now physicians will realize that statin therapy is first-line, with other drugs being used as an add on, if necessary, to lower the number of atherogenic particles.

The 3,414 patients in the study were randomized to statin or to statin plus niacin therapy. The age was 64 ± 9 years, 85% were men and all had documented arteriosclerotic vascular disease. Statin therapy had been used in 94% for some period of time before enrollment. The mean LDL-C was 71 mg/dL, HDL-C 34.9 mg/dL and triglycerides 161 mg/dL at randomization to the treatment regimens. Therefore, these were patients at very high risk for CHD already treated to aggressive LDL and non-HDL targets.

The National Lipid Association stated in a recent release, "The findings of AIM-HIGH will require careful study to determine if there are specific reasons for the failure of niacin to provide incremental risk reduction in this population of patients. We have much to learn on such therapeutic strategies and the value of targets beyond LDL-C."

Dr. Richman reminds patients that discontinuing cholesterol-lowering therapy is the wrong action and should not be done without the advice of a physician who specializes in lipid disorders. For more information, you can go to my website at www.lipidcenter.com