Surprises and reaffirmations in 2008 clinical trials

Several clinical trials published last year may ultimately shape the way we practice medicine. Some of the findings were surprises that prompted us to rethink some of the basic tenets of our clinical practice, but others reaffirmed our practice patterns.

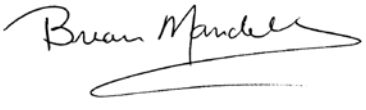
The ACCORD trial (Action to Control Cardiovascular Risk in Diabetes) investigated very aggressive glucose control in type 2 diabetes. To our surprise, it did not extend the findings of earlier landmark trials that had showed marked microvascular benefits with modestly aggressive glucose control. Instead, as discussed by Dr. Byron Hoogwerf in our October 2008 issue (www.ccjm.org/content/75/10/729.full), the ACCORD trial found that more patients died who underwent the extremely aggressive glucose-control strategy.

Like the ACCORD trial, the JUPITER trial (Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin) examined how far you can pharmacologically lower a causative factor—in this case, low-density lipoprotein cholesterol (LDL-C)—without causing adverse effects. In this month's issue (page 37), Drs. Shishehbor and Hazen discuss the results of the JUPITER trial, in which "healthy" patients with LCL-C levels lower than 130 mg/dL and elevated high-sensitivity C-reactive protein (hs-CRP) levels were aggressively treated with rosuvastatin (Crestor). The median LDL-C level fell from 108 to 55 mg/dL, and the trial was stopped early when the number of predefined cardiovascular events was found to be 44% lower in the treated group than in the placebo group.

The efficacy result is not that surprising—there is probably no specific LDL-C number that should trigger a decision to treat. Furthermore, in JUPITER, unlike in ACCORD, there was no downside to the aggressive treatment that outweighed the benefits. The acute-phase reactant hs-CRP (or the company it kept, ie, metabolic syndrome) was a useful marker in identifying patients at risk of cardiovascular events, thus permitting the earlier-than-expected outcome differences. But the study does not resolve the question of whether hs-CRP is pathogenic in its own right.

So, as we begin 2009, we know that too much glucose is bad, but trying too hard to lower it in type 2 diabetes may be worse. We start the new year with a reaffirmation of the LDL-C hypothesis: LDL-C promotes cardiovascular morbidity, and starts to do so even when the person is apparently healthy. I am still not convinced that hs-CRP is an active player in the pathogenesis of atherogenesis, but that is a study for another year.

On behalf of the editorial staff of the *Journal*, I wish you all a happy, healthy, and most of all more peaceful 2009.



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