Statins Offer No Benefit in Chronic Heart Failure

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MUNICH — Rosuvastatin at 10 mg per-day had no impact on clinical outcomes in patients with chronic heart failure in a large clinical trial.

Results of the GISSI-HF trial, in which 4,574 Italian patients with chronic heart failure were randomized double blind to the statin or placebo and followed for a median of 3.9 years, suggest that there is no indication for giving statins as a treatment for heart failure, Dr. Gianni Tognoni said at the annual congress of the European Society of Cardiology.

He noted that this is the second large clinical trial that has failed to show a mortality benefit for statin therapy in patients with symptomatic chronic heart failure. The GISSI-HF trial follows the 5,011-patient Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA), which featured 33 months of follow-up in a population with a history of ischemic heart disease (N. Engl. J. Med.;357:2248-61).

In GISSI-HF, all-cause mortality was 29% in the rosuvastatin (Crestor) group and 28% with placebo. The other primary end point—death or hospitalization for cardiovascular reasons—occurred in 57% of statin-treated patients and 56% on placebo, according to Dr. Tognoni, cochair of the GISSI-HF steering committee and professor of cardiology at the Mario Negri Research Institute South, Chieti, Italy. Both differences were statistically nonsignificant.

The GISSI-HF was a nested study designed to test two hypotheses. Unlike the statin hypothesis, the other one—that a once-daily, low-dose, fish oil capsule would reduce morbidity and mortality in patients with symptomatic chronic heart failure—was supported by the findings (see accompanying story, p. 1). The only GISSI-HF participants in the larger fish oil study who weren't randomized to rosuvastatin or placebo were already on a statin or had a contraindication.

Discussant Dr. Philip Poole-Wilson commented that he found GISSI-HF persuasive and generalizable, particularly taken together with CORONA. The findings are surprising and disappointing in light of

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DR. TOGNONI

the much-discussed pleiotropic effects of statins, which now appear to be clinically irrelevant in the setting of heart failure.

The trials, he said, contain a valuable lesson: "GISSI-HF has refuted many observational studies, and yet again meta-analyses have been shown to be wanting. They all predicted a positive outcome. And there were even those who said that the CORONA study and this study were unethical because it was so obvious that statins would be beneficial; they were wrong," declared Dr. Poole-Wilson, professor of cardiology and head of cardiac medicine at the National Heart and Lung Institute, Imperial College, London.

The GISSI-HF trial indicates patients with symptomatic heart failure should not be started on a statin. That's obvious. But the studies also raise several new controversies, he continued.

"If a patient has severe heart failure and is already on a statin, are you going to withdraw it? The trial didn't actually address that question, yet we have to make a judgment. My judgment is that the answer is probably yes," Dr. Poole-Wilson said.

Similarly, he would now be inclined not to start a statin in an asymptomatic patient with New York Heart Association class I heart failure, although that's a decision that needs to be individualized.

There is, however, overwhelming evidence that statins are beneficial in patients with coronary heart disease but who don't have heart failure.

"And one of these benefits is to reduce new-onset heart failure. So all of those patients must be started and maintained on a statin," Dr. Poole-Wilson emphasized.

The GISSI-HF trial was funded by the Societa Prodotti Antibiotica, Pfizer Inc., Sigma Tau, and AstraZeneca Pharmaceuticals, which provided Dr. Tognoni with research support and honoraria. The trial was simultaneously published online (Lancet 2008 Aug. 31 [doi:10.1016;50140-6736(08)61240-4]). ■