

No CV Benefit from Rosuvastatin in Dialysis

BY MICHELE G. SULLIVAN

While rosuvastatin significantly improved the lipid profile of patients with end-stage renal disease, those improvements did not translate into a decrease in the combined rate of heart attack, stroke, or cardiovascular death, a large randomized, controlled trial has confirmed.

"Although the patients tolerated the treatment very well, and it did lower their low-density lipoprotein by the expected amount, rosuvastatin had absolutely no treatment effect on either the composite cardiovascular end point or any of our secondary end points," Dr. Bengt Fellstrom said at a teleconference held at the annual meeting of the American College of Cardiology.

"We suspect very strongly that the vascular disease they have is quite different from that in patients without end-stage renal disease. It has more to do with endothelial dysfunction and calcification, while cholesterol is not a significant risk factor," Dr. Fellstrom said.

The 4-year AURORA study randomized 2,776 patients, all of whom had been on regular hemodialysis for at least 3 months, to either rosuvastatin 10 mg per day or placebo. The study's primary end points were time to nonfatal heart attack or stroke, or cardiovascular death. Secondary end points included all-cause mortality, event-free survival, and coronary or peripheral revascularization.

The patients' mean age was 64 years. At baseline, their average total cholesterol level was 175 mg/dL, with an LDL level of 99 mg/dL and HDL level of 45 mg/dL.

By 3 months, patients on rosuvastatin experienced a significantly larger decrease in LDL cholesterol than those taking placebo (43% vs. 2%, respectively). Rosuvastatin also significantly reduced total cholesterol (27% vs. 0.5%, respectively) and triglycerides (16% vs. an increase of 0.9% in placebo group). HDL increased in the active treatment group, but not significantly so.

The primary end point of stroke, heart attack, or death from those causes occurred in 396 patients taking the study drug and 408 taking placebo—not a significant difference. Neither were there any significant differences when the investigators examined the primary end points individually.

Death for any reason occurred in 636 patients taking rosuvastatin and 660 taking placebo, again not a significant difference. None of the prespecified secondary outcomes were significantly affected by the study drug.

The findings echo those of the German Diabetes and Dialysis study, which found that atorvastatin conferred no cardiovascular benefits on dialyzed patients with type 2 diabetes.

"Since that didn't work either, I suspect this is a class effect for all statins," said Dr. Fellstrom of the University Hospital, Uppsala, Sweden.

AURORA enrolled only statin-naive patients. Dr. Fellstrom noted that the drugs

do have an important place in the care of many other patients with end-stage renal disease. "Up to 40% of these patients have been put on statins before going on dialysis, after having a coronary event. Those patients should stay on the treatment."

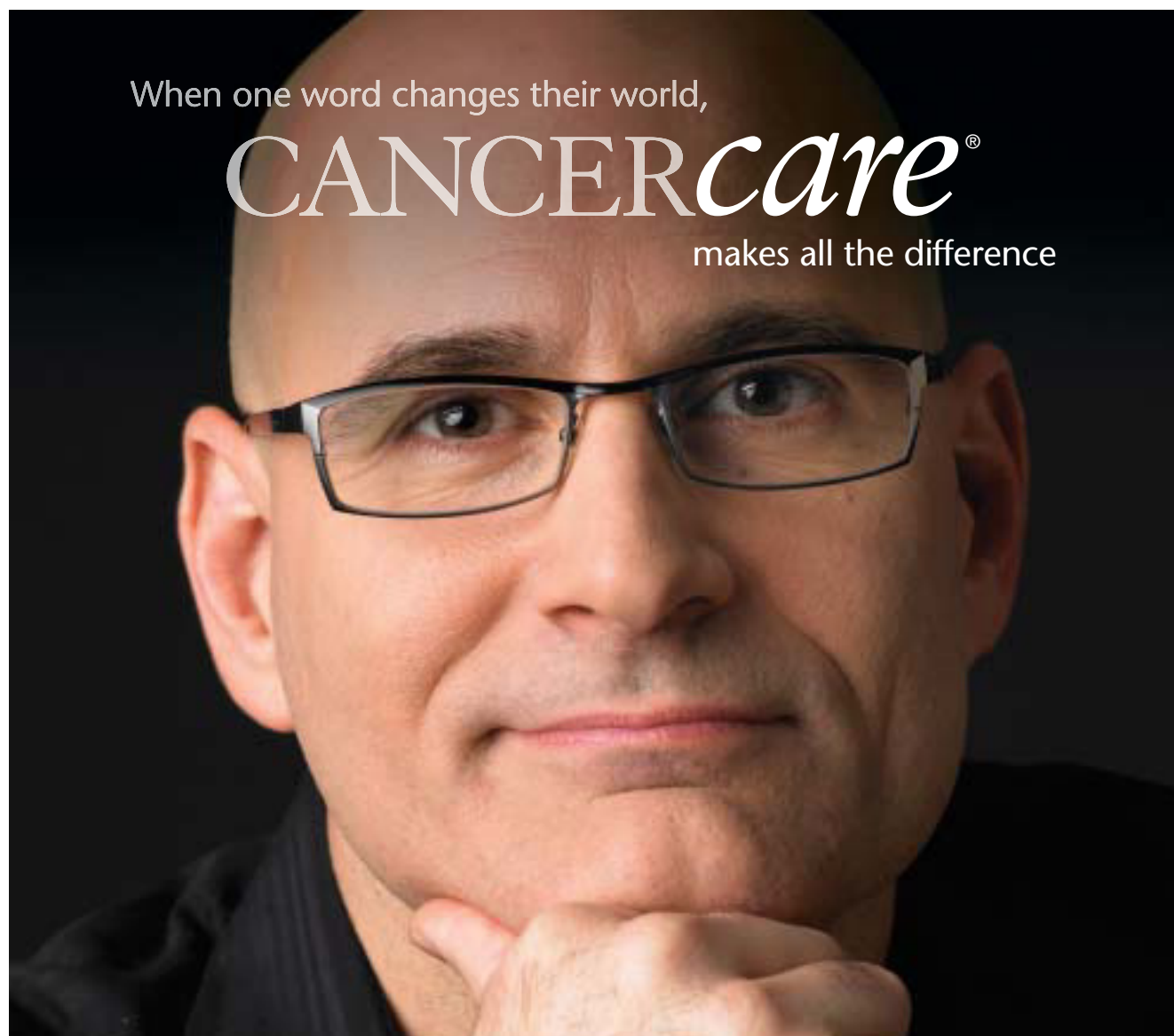
The study was published simultaneously online in the *New England Journal of Medicine* (doi:10.1056/NEJMoa0810177). An accompanying editorial discussed the disappointing find-

ing that yet another possible intervention for improving cardiovascular survival in dialyzed patients had failed (doi:10.1056/NEJMe0901067).

"AURORA has shown that the hope of effective interventions to lower cardiovascular risk among patients undergoing hemodialysis remains unrealized," wrote Jonathan C. Craig, Ph.D., of the University of Sydney, Australia. "The search is on for more promising interventions for

a desperately needy group of people with very poor outcomes. Such interventions need to be based on a more complete understanding of the causal pathway of cardiac disease in patients undergoing dialysis."

Dr. Fellstrom reported receiving consulting fees from Astra-Zeneca, the maker of rosuvastatin (Crestor), and other large pharmaceutical companies. Dr. Craig reported no conflict of interest. ■



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