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CORRESPONDENCE: LETTER TO THE EDITOR

High-Dose Statin, Not So IDEAL?

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Tikkanen et al. (1) present an interesting post-hoc analysis of the IDEAL (Incremental Decrease in Endpoints Through Aggressive Lipid Lowering) study with a novel statistical method using all vascular rather than just the first cardiovascular event recorded, and they propose highly significant p values in support of using top-dose atorvastatin (80 mg/day) versus "standard" dose simvastatin (20 mg/day or uptitrated). The authors propose that such a statistical approach is of value because of the health economic importance of subsequent events, and that their results "suggest that clinicians should not hesitate to prescribe high-dose statin therapy for patients experiencing multiple recurrent cardiovascular events."

The background: The IDEAL study was an apparently well-run, open-label drug comparison trial in all post-myocardial infarct (MI) patients, of whom about 40% had already experienced revascularization and an 8.3% mortality rate ($\pm 0.1\%$ between groups) during the mean 4.8 years of follow-up. The lack of mortality benefit is in line with atorvastatin's well-known inability to lower mortality, with the notable findings of the TNT (Treating to New Targets) trial and the SPARCL (Stroke Prevention by Aggressive Reduction in Cholesterol Levels) trial that ended with numerically more deaths on top-dose atorvastatin than on low-dose and placebo, respectively (2,3).

Since mortality is not reduced, we have to ask about the nature of events prevented. The authors report that the first, second, and third events recorded were 46%, 51%, and 43% on the basis of decisions to hospitalize or to revascularize, whereas nonfatal MIs represented only 18%, 15%, and 15%, respectively. The ASCOT (Anglo-Scandinavian Cardiac Outcomes Trial) study found angina reduced by 41%, likely by the nitric oxide/endothelial nitric oxide synthase nitroglycerin mimicking action that all statins share (4,5). The amount of angina experienced is a factor potentially affecting the medical decisions and the number of MIs recorded in a trial.

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Thus, we have to be careful including these softer end points, and since the authors bring up health economics, we should be aware that at the current (Vermont) retail prices of \$5 per pill for "high dose-statin" (Lipitor 80 mg and Crestor 20 mg), it would cost, as an example, from \$560,000 to \$1,160,000—slightly less in men, more in women—to prevent either a revascularization, stroke, or MI on the basis of the results of the recent JUPITER (Justification for the Use of Statins in Primary Prevention: An Intervention Trial Evaluating Rosuvastatin) primary prevention study (rosuvastatin 20 mg vs. placebo) (6). Even at the current Vermont price for generic lovastatin (\$0.78 for 20 mg), such costs, likely even in secondary prevention, may be many times those of an angioplasty, a hospitalization for angina, or the cost of a (not clearly defined nor quantified by Tikkanen et al. [1]) peripheral vascular disease event.

These drug costs call into question the benefit of statins, including high-dose statin, regarding health economic benefits. Therefore, could the authors comment on the health economic effects of their expanded end point analysis, and provide numbers needed to treat for individual end points, with confidence intervals?

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