of drugs within a particular group, such as statins, as per large randomized clinical trials, a surrogate end point simply cannot be used to claim a superior efficacy for the only drug (rosuvastatin) without any evidence of efficacy in terms of morbimortality.

Cost-effectiveness analysis is a very useful tool for decision-makers to allocate properly available resources. However, if it is not correctly conducted or if it is performed with inappropriate data, it is possible that at the end decision-makers may make incorrect decisions with the consequent being ineffective allocation of resources. Therefore, we believe that rosuvastatin should demonstrate efficacy in terms of morbimortality before trying to demonstrate cost-effectiveness.

For these reasons, we do think that this cost-effectiveness analysis should be considered a preliminary exploratory exercise, pending on the results of morbimortality. Otherwise, conclusions are potentially misleading for decision-makers.—Javier Soto, MD, PhD, and Jaime Fernandez de Bobadilla, MD, Health Outcomes Research, Medical Unit, Pfizer, Madrid, Spain.

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The authors reply . . .

Formulary Decision-Making Should Rely on the Best Available Evidence

To the Editor—Evidence of effectiveness and cost-effectiveness is inherently dynamic in nature. Cost-effectiveness models based on the best data available at the time are an important contribution to evidence-based decision-making if they reveal the likely outcomes of various scenarios and quantify the degree of uncertainty around the apparently optimal approach. Cost-effectiveness models also illustrate the trade-offs inherent in each potential alternative available to the decision-maker and should be updated as new evidence becomes available.

In 2000, The Academy of Managed Care Pharmacy issued its first Format for Formulary Submissions, which provided US payers with a new tool to proactively request clinical and economic data from health technology manufacturers. The Format, which has been revised substantially in recent years, is now used by health-care organizations covering some 150 million lives in the United States [1]. This guidance recommends that dossiers for new drug products be requested by health plans approximately 6 months before launch, and explicitly calls for the use of economic models “to inform decisions about the value or cost-effectiveness of pharmaceuticals, biologics, and vaccines.” Such models are to be based on
International Society for Pharmacoeconomics and Outcomes Research (ISPOR)’s Good Research Practices—Modeling Studies [2], which stipulate that data sources be “clearly defined and from the most recent studies.”

Our model did not extrapolate the intermediate end-points of cholesterol reduction and National Cholesterol Education Program Adult Treatment Panel II goal achievement to long-term reductions in coronary heart disease (CHD) events and mortality, for three reasons: First, the best available head-to-head statin trials that included rosuvastatin as a comparator—and therefore the time horizon of our primary analysis—were limited to 1 year. Second, extrapolating to long-term outcomes would have required us to assume a “class effect” among the statins by employing the well-described relationship between lipid-lowering and event reduction [3], and this would not have changed our findings because incremental lipid-lowering would yield incremental risk reduction. Third, there is a precedent for publishing such “short-term” evaluations of other statins [4–9].

We believe our analysis informs near-term decisions about statin formulary placement in the spirit of Academy of Manager Care Pharmacy and ISPOR guidance, using the best data available at the time our analysis was conducted in early 2005. The full conclusion of our analysis was that rosuvastatin dominates atorvastatin, pravastatin and branded simvastatin, and it may be considered cost-effective compared with generic lovastatin [10]. We acknowledged in our article that long-term trials have documented the risk-reducing capacity of each of the comparator products, and we recommended that decisions based on our model be reconsidered when long-term effectiveness and safety data become available for rosuvastatin.

The strategy tacitly advocated by Drs Soto and Bobadilla is to use only older statins until long-term rosuvastatin trials are completed. Our analysis quantified the trade-offs associated with that strategy. The results indicate that the opportunity cost could be substantial due to the lower average cost and greater LDL-C lowering potential of rosuvastatin compared to atorvastatin, pravastatin, and simvastatin.

Our analysis did assume that adverse event rates would be similar across the class, based on clinical trial evidence available at the time. The recent article by Alsheikh-Ali and colleagues [11] does not conclude that spontaneous adverse event reports (AERs) are indicative of actual rates, and the authors acknowledge that external factors such as media coverage and available doses may explain differences in spontaneous AER. After careful review of the same AERs, the Food and Drug Administration concluded that “Crestor (rosuvastatin) does not pose a risk of muscle toxicity greater than that of other approved statins. With respect to renal toxicity, there is no convincing evidence that Crestor poses a risk of serious renal injury [12].” We did not include C-reactive protein (CRP) reduction as a measure of efficacy in our analysis because data were not available for rosuvastatin at the time. Although the importance of CRP and other inflammatory markers as independent risk factors for CHD is currently a topic of intense study, current treatment guidelines do not identify CRP as a target of therapy [13,14] and statins are not indicated for the reduction of CRP. The objective of treatment remains LDL-C reduction [13].

In conclusion, we encourage managed care decision-makers to consider carefully and critically all of the evidence available for any product at the time of its launch. The most valuable decision tools are those that illustrate the risks, benefits, and trade-offs of potential decisions, including the opportunity cost of waiting for more data. Information available at the time of launch will inevitably be incomplete, but it can also be profoundly helpful to decision-makers who interpret the results in light of the limitations and commit to updating decisions when new data warrant.—Joshua S. Benner PharmD, ScD, Timothy W. Smith, David Klingman, PhD, Jonathan C. Tierce CPhl, ValueMedics Research, Falls Church, VA, USA; C. Daniel Mullins PhD, University of Maryland, Baltimore, MD, USA; Ned Pethick, AstraZeneca, Wilmington, DE, USA; and John C. O’Donnell PhD, AstraZeneca, Macclesfield, UK.

References


