LIPITOR VS. SIMVASTATIN FOR EFFICACY OF CARDIOVASCULAR EVENT AND MORTALITY REDUCTION

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Millions of Americans have hypercholesterolemia, placing them at excess risk for cardiovascular disease. As a result, patients desire affordable, effective methods to help combat high cholesterol with HMG-CoA reductase inhibitors (statins). Both Lipitor (branded medication) and simvastatin (generic medication) are drugs that reduce blood cholesterol levels. Several randomized control trials have been conducted to determine their long-term cardiovascular disease event reduction in patients with elevated LDL levels. Hypothesis: Is there any additional cardiovascular benefit for subjects taking the branded product Lipitor when compared to simvastatin? A search was performed utilizing the *Ovid Medline*, *Pubmed*, and the Internet to conduct a systematic review. Search terms were limited to: clinical trials, statin comparisons, and cardiovascular disease. Several of the eligible articles directly compared cholesterol levels and cardiovascular outcomes in Lipitor- and simvastatin-treated patients at specific time intervals.

INTRODUCTION

In 2008, an estimated 770,000 Americans were diagnosed with a new coronary heart disease (CHD), the most widespread form of heart disease in the United States. Recently, the National Health and Nutrition Examination Survey reported high hypercholesterolemia levels in the general population and generally higher levels among minority populations. As a result, many individuals and their healthcare providers desire appropriate lipid-lowering methods to help combat hypercholesterolemia.

Last year a comprehensive systematic study was conducted to determine the efficacy of the low-carbohydrate Atkins diet vs the low-fat American Heart Association diet in reducing high cholesterol in at-risk patients. Although a major component of serum cholesterol is derived from food intake, the body naturally makes 80% of total cholesterol.[1] As a result, many people still need cholesterol-lowering medications in addition to healthy diet and positive lifestyle changes. Lipitor and simvastatin are two widely prescribed hydroxymethylglutaryl-coenzyme-A reductase inhibitors (statins) that have been shown to improve serum cholesterol by halting the construction of that key cholesterol-producing enzyme.

Lipitor (atorvastatin), a statin marketed by Pfizer, has been clinically proven to reduce the threat of stroke and heart attack in patients with risk factors for cardiovascular disease such as smoking or family history. Lipitor is the largest selling drug in the world with 2006 profits totaling >$12 billion.[2]

Simvastatin is another widely used hypolipidemic drug used to reduce the risk of heart disease. Simvastatin, which was marketed by Merck as the branded form of Zocor, is the second best selling drug in America, with annual sales >$5 billion.[3] This statin is synthetically derived from a fermentation product of *Aspergillus terreus*. After oral ingestion, simvastatin is hydrolyzed to the corresponding β-hydroxyacid form, which blocks HMG-CoA reductase. As in the case of people taking Lipitor, patients considering simvastatin should discuss preexisting conditions with their physicians and continue positive lifestyle choices such as diet, weight loss, and exercise in order to obtain optimal results.[4]

Numerous randomized control trials have been conducted to determine the long-term efficacy of branded Lipitor and generic simvastatin in improving factors such as LDL-C, HDL-C, and triglyceride levels. However, the effectiveness of these statins for long-term cardiovascular event prevention and survival in hyperlipidemic patients remains largely unknown. Therefore, a systematic review was conducted to determine the direct correlation between improved serum cholesterol levels and reduced cardiovascular disease events for each drug. I wanted to answer the research question: Is there any additional cardiovascular benefit for subjects taking the branded product Lipitor when compared to simvastatin?

METHODS

I used Lipitor's official website[5] and the primary web page for ZOCOR (simvastatin)[6] to gather primary information pertaining to the purpose and chemical components of each statin. A Pubmed and Ovid MEDLINE search

Table 1. Comparison of clinical trials exploring the efficacy of simvastatin vs atorvastatin

	Simvastatin Studies				Atorvastatin Studies			
	Simva-A 20 mg	Placebo	Simva-B 40 mg	Placebo	Atorva-A 10 mg	Placebo	Atorva-B 10 mg	Placebo
N	2221	2223	10269	10267	1428	1410	5168	5137
Primary Endpoint	182 (8%)	256 (12%)	1328 (12.9%)	1507 (14.7%)	83 (5.8%)	127 (9.0%)	100 (1.9%)	154 (3.0%)

was conducted to compile information on randomized control studies comparing the efficacy of both medications for long-term prevention of cardiovascular events and death. Searches were performed for articles published between January 1, 2004, and July 1, 2008. Search terms were limited to: clinical trials, statin comparisons, and cardiovascular disease. Several of the eligible articles directly compared cholesterol levels and cardiovascular outcomes in Lipitor and simvastatin patients at specific time intervals. One of the 19 eligible articles[7] was a meta-analysis that yielded additional references for simvastatin and atorvastatin trials. These 4 trials were examined to extrapolate data on the efficacy for each statin.

RESULTS

Simvastatin Study A[8]

The Scandinavian Simvastatin Survival Study (4S) was designed to test the notion that cholesterol reduction with simvastatin can lower mortality and cardiovascular incident rates in individuals with CHD. 4444 patients with angina pectoris or previous myocardial infarction and total cholesterol between 213–310 mg/dl while treated with a lipid-lowering diet were randomly assigned to a double-blind treatment with simvastatin or placebo. Total mortality was the primary endpoint over the 5.4 years of median follow-up.

Simvastatin Study B[9]

The MRC medical research council/BHF Heart Protection Study investigated 20536 United Kingdom adults (aged 40–80 years) with coronary disease or diabetes who were randomly allocated to receive 40 mg simvastatin daily or matching placebo for 5 years. Primary outcomes were mortality (for overall analyses) and fatal or non-fatal vascular events (for subcategory examination).

Atorvastatin Study A[10]

The Collaborative Atorvastatin Diabetes Study (CARDS) aimed to assess the effectiveness of atorvastatin 10 mg daily for primary prevention of major cardiovascular events in patients with type 2 diabetes. Within 132 UK and Ireland centers, 2838 patients (aged 40–75 years) were randomized to placebo or atorvastatin 10 mg daily. Participants had no documented previous history of CHD, and LDL-C concentration of 4.14 mmol/L or lower. The primary endpoint was time to initial incident of the following: stroke, acute coronary heart disease events, or coronary revascularization.

Atorvastatin Study B[11]

The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) was designed to compare two cholesterol lowering treatment strategies and atorvastatin vs placebo in 19,342 high-risk patients (aged 40–79 years) who had no history of CHD. Serum cholesterol concentrations were 6.5 mmol/L or lower. The primary endpoint was non-fatal myocardial infarction and fatal CHD.

Table 1 displays the comparative results for each study.

DISCUSSION/CONCLUSION

All participants in the simvastatin trials had elevated serum cholesterol levels and either coronary heart disease or diabetes. By comparison, individuals in each atorvastain study had no documented history of cardiovascular disease, average or optimal cholesterol concentrations, and were only at moderate risk for developing cardiovascular events. Compared with placebo, simvastatin obtained a range of (12.2%–33.3%) event reduction in a population with coronary disease or diabetes. By comparison, atorvastatin obtained a (35.5%–36.6%) range reduction in primary endpoint events in a population with a lower burden of pre-existing cardiovascular disease. Thus, while both agents demonstrate benefit, the populations each drug examined were quite different. The goal of this analysis was to determine the best therapeutic option after lifestyle modification. For the studies we reviewed, it appears that both drugs provide benefit but individuals taking branded Lipitor (atorvastatin) have greater probability of benefit and predictability of cardiovascular risk reduction. The evidence for simvastatin must be extrapolated from data on a population with higher levels of disease. Although simvastatin has the potential to produce similar effects, the randomized controlled trials only showcase its efficacy in more diseased populations, which make up the minority in the United States. Patients who fall into the health categories studied in this systematic review should use these results as primary information before consulting their healthcare providers on appropriate statin treatment.

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