A Comparison of the Cholesterol-lowering Drugs Zocor® (simvastatin) and Crestor® (rosuvastatin) for James *****’s Post-operative Treatment Plan

A Recommendation Report Prepared for:

Dr. James *****
Professor, Chemical Engineering

and

Mr. Paul Kellermann
English 202C Instructor

By Catherine *****

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- This recommendation report compares the usefulness of the cholesterol lowering drugs Zocor® (simvastatin) and Crestor® (rosuvastatin) to James *****’s post-operative treatment plan. The drugs were compared based on 4 criteria: primary effectiveness at reducing LDL levels; secondary effectiveness at improving other risk factors; severity of drug side effects; and practicality of use. Supporting material was collected primarily from published clinical trials. At the end of the report, an overall conclusion and a list of recommendations for the future are provided. At the very beginning of the report, an executive summary of the report findings is provided.
EXECUTIVE SUMMARY

With your recent heart attack and coronary bypass surgery, you have begun a prevention plan that involves the cholesterol-lowering statin simvastatin, marketed under the brand name Zocor. However, you wanted to know if the new type of statin, rosuvastatin (brand name Crestor) would be a better choice.

Based on your blood lipid profile, the most important goal of your drug regimen is to lower your LDL levels. Rosuvastatin is able to lower blood LDL levels more effectively than simvastatin, allowing for a decrease in LDL levels as high as 45% in some cases. Reductions of this size would help you achieve your primary goal, an LDL level below 100 mg/dL. Rosuvastatin also outperforms simvastatin in secondary effectiveness characteristics, showing greater improvements in HDL and apo-B levels in clinical trials. Both drugs appear to block one major trigger of plaque formation, inflammation in the arteries, in more qualitative studies.

Although each drug has mild side effects, the potential for serious muscle or liver problems is small, and most effects are reported in fewer than 4% of patients. The effectiveness of simavastatin has been determined in long-term studies, but only short-term studies are available for rosuvastatin. The hydrophilic chemical nature of rosuvastatin suggests that it may ultimately be safer and have less drug-drug interactions than the hydrophobic simvastatin. Despite the new status of Crestor on the world market, the smaller necessary dosage means it may be cheaper to use, with fewer side effects. Crestor also provides a greater flexibility of dosage and thus the potential for success at lowering your cholesterol.

Crestor is a more effective, potent, and useful form of a cholesterol-lowering drug, and it meets your specific post-operative needs. Although you will not be able to start on a Crestor regimen immediately, once the drug is released to U.S. markets, you should ask you doctor if you can switch to Crestor.
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INTRODUCTION

Recently, you suffered a heart attack and, subsequently, had a quaternary bypass operation due to a high degree of atherosclerotic blockage in your arteries. From personal discussions, I know that one of your top priorities right now is to avoid further heart attacks, strokes, and the need for additional invasive procedures. You already have a dietary and exercise plan in place to aid in reducing your cholesterol level to a suitable number for a coronary disease patient, but, to drop your cholesterol levels even more, your doctor has prescribed the drug Zocor®. This drug, which is manufactured by Merck, is the medication suggested for use by doctors in your HMO plan.

However, Zocor is only one of many cholesterol-lowering medications on the market. Other regimens include gemfibrozil, a fibroid treatment, and high doses of the vitamin niacin. The most frequently prescribed drug for patients interested in lowering their cholesterol is Lipitor® (27). Lipitor and Zocor have been shown to possess similar cholesterol-lowering effects. Recently, however, you read an article claiming that the most effective cholesterol-lowering drug on the market was Crestor®, manufactured by AstraZeneca. Both Crestor and Zocor belong to a class of drugs called the statins. Crestor’s active ingredient is rosuvastatin, while Zocor’s active ingredient is simvastatin. Both chemicals have a similar chemical structure, and they both work in a similar fashion. Statins inhibit a cellular enzyme called HMG-CoA reductase that is used to synthesize cholesterol molecules from metabolic precursors (27). Thus, by blocking the cellular synthesis of cholesterol, the level of blood cholesterol should go down, and a smaller buildup of fatty deposits on your arteries would be expected. Both Zocor and Crestor claim to reduce blood cholesterol levels as well as to reduce the frequency of heart attack and stroke.

Currently, only Zocor, and not Crestor, is available in the United States. Crestor has been approved in Canada and Europe, and a new drug submission form for Crestor was submitted to the U.S. FDA in early 2001. The FDA is expected to place Crestor on the U.S. market in the next couple of months, so, by this summer, you will likely have the option of switching to Crestor or remaining on Zocor. However, it is difficult to ascertain similarities and differences between these two drugs just from the package inserts (the Crestor insert is available online). I have a strong interest in maintaining your well being, so I have decided to use my college background in biochemistry to research cholesterol-lowering drugs for you. In this report, I will compare the characteristics and effectiveness of Zocor and Crestor to determine if you should continue taking Zocor, or if you should switch to Crestor as part of your regimen.

To research this question, I examined the results of clinical trials published in top medical journals. This kind of research allowed me to separate generalized claims from actual facts. Since each company is looking to increase sales of their particular drug, I was wary of information provided in package inserts and drug web sites and focused on statistical data in journal articles. However, I did incorporate dosage information and precautions described in the Zocor and Crestor patient information sheets. For this report, I will compare the two drugs based on 4 different criteria. First, I will compare their effectiveness in lowering LDL cholesterol levels, the primary goal of your post-operative plan. Next, I will compare their effectiveness in improving secondary factors in cardiovascular disease management, namely HDL levels, apolipoprotein levels, and...
inflammation response. Third, I will compare the severity of their side effects. Finally, I will compare their practicality of use, incorporating ease of dosage, annual cost, and flexibility of dosage. Since you are a researcher, like me, I know you are interested in the whole story behind each medication. You will be happy to find that I have included sufficient detail behind the clinical trials I reference. At the end of the report, I will provide an overall summary of the findings and present a list of my recommendations for your future treatment plan.
COMPARISON OF THE DRUGS

(I). Primary Effectiveness: Lowering Blood LDL Levels

Introduction

Ever since the onset of your heart attack, I know you have been exposed to many printed and online materials explaining the link between blood cholesterol levels and an increased occurrence of atherosclerosis. As you know, your body obtains cholesterol from both the foods you eat and from synthesis of cholesterol molecules within the body’s cells; statins like Zocor and Crestor inhibit the latter source of high cholesterol. In general, cholesterol levels higher than 200 mg/dL are considered to put you at risk for heart disease (25). However, high total cholesterol levels do not necessarily lead to clogged arteries. Your LDL (low-density lipoprotein) level is the most important number, as it is a predictor of the severity of future blockage and coronary artery disease. LDL complexes carry cholesterol from your liver to your heart, where fatty plaques can form. The current consensus on LDL levels is that the lower the levels, the better (26). The magnitude of an LDL reading is directly correlated with the incidence of heart attack and mortality from coronary artery disease.

Based on cholesterol readings from your last doctor’s visit before you began Zocor dosage, you had an LDL level of 138 mg/dL. According to levels set by the NCEP ATP (National Cholesterol Education Program-Adult Treatment Panel), this level would be acceptable for a typical healthy adult with no risk factors (25). Since you are a coronary disease patient, you should aim to reduce your LDL level to 100 mg/dL; this would require a reduction of 28%. By reducing LDL levels, you will also lower your overall blood cholesterol concentration, although, at 170 mg/dL total blood cholesterol, you are well under the danger limit of 200 mg/dL. A change in diet alone has been shown to be able to reduce blood LDL levels as much as 20-25 % (25). However, this percentage varies from person to person, and, based on my personal observations of your pre-heart attack diet, you were not consuming excess amounts of foods high in cholesterol or saturated fats. Therefore, due to the prime importance of LDL reduction and the large percentage reduction in LDL levels that you need to achieve, a drug that lowers your LDL level is a priority for your post-operative regimen. In this section of the report, I compare the ability of rosuvastatin (in Crestor) and simvastatin (in Zocor) to reduce serum LDL levels. First, I will present data from general trials, and, next, I will present data relating to your particular personal characteristics.

General Trials

Since simvastatin has been on the market for several years, a wide variety of studies have been conducted to determine its cholesterol-lowering effects. Many fewer rosuvastatin-only trials have been conducted. For the most effective comparison of the two drugs, however, clinical trials that compare both drugs in the same experimental setup are the most relevant. In these initial trials, effectiveness was measured in two
ways, either by the ability of patients to reach NCEP ATP cholesterol goals or by the percent decrease in patient blood LDL levels. In a trial at the University of Scotland involving people with hypercholesterolemia, participants were provided with 5 or 10 mg doses of rosuvastatin or 20 mg doses (equivalent to your current dose) of simvastatin (23). 86% of patients were able to reach their ATP-dictated cholesterol goal in 12 weeks with either dose of rosuvastatin, as compared to 64% of the patients taking simvastatin; this is a 22% improvement. In a different 1-year trial comparing 10 mg and 20 mg doses of rosvastatin and simvastatin, respectively, the same pattern was obtained. 88% of rosuvastatin patients were able to achieve their goal, as opposed to 73% of simvastatin patients; this is a 15% improvement (5).

The same favorable results were observed for rosuvastatin’s ability to lower LDL numbers. The most straightforward way to quantify this decrease is through raw percentage decreases. AstroZeneca, the company that manufactures Crestor, conducted a 12-week clinical trial on hypercholesterolemic patients (3). Since this was a randomized, double-blind study, it can be considered as valid as any of the other clinical trials, despite the company affiliation. Patients on 5 and 10 mg/dL regiments of rosuvastatin exhibited LDL decreases of 40.6% and 48.1%, respectively, as compared to decreases of 27% in patients on 20 mg of simvastatin; this is a 20% improvement. Another way of quantifying LDL decreases is through decreases in the LDL/HDL blood cholesterol ratio. In a 12-week clinical trial at the University of Pennsylvania, decreases in LDL/HDL ratios were computed for hypercholesterolemic patients (21). Patients on 10 mg/dL rosuvastatin exhibited decreases of 52% as compared to patients on 20 mg simvastatin, who exhibited decreases of only 39%; this is a 13% improvement.

**Specific Information From Trials**

Each of the aforementioned clinical trials provides data for all groups involved in the trials—male and female, young and old. You may be wondering if all of these generalizations apply to you. The aforementioned AstroZeneca trial included patients with hypertension and atherosclerosis, both of which are conditions you currently face, and typical improvement rates were observed for this group (3). A different AstroZeneca trial in the United Kingdom determined that similar results were obtained from rosuvastatin in both males and females and in both the young (18-35) and the elderly (over 65) (15). Since you fall into the >65 age bracket, this study suggests that rosuvastatin will be effective in your body. This latter AstroZeneca study differed from all of the other trials, however, in that 40 mg doses were distributed and healthy individuals were used at the beginning of the study. The cholesterol levels in healthy individuals would actually represent you more accurately, since your LDL and total cholesterol levels fall within the normal range. It is possible, and perhaps even likely, that the largest decreases in LDL levels are seen for the hypercholesterolemic patients and that you personally will not see such large reductions in your blood cholesterol levels from either statin. Unfortunately, no raw percentages for the change in LDL levels were presented in this paper for comparison. For a comparison of the drugs that would truly relate to your situation, a trial of coronary disease patients with relatively normal LDL levels would be needed.
Conclusion

The results of multiple clinical trials suggest that Crestor, with the active compound rosuvastatin, is significantly more effective than your current drug Zocor, with the active compound simvastatin, in patients with high cholesterol. Despite the lack of clinical trials exactly matching your situation, rosuvastatin does exhibit the same increase in benefits in men of your age bracket and in fellow patients with hypertension and atherosclerosis. With the potential to reduce LDL levels as much as 48% in some patients, rosuvastatin should be able to help you achieve your goal of 100 mg/dL LDL easily. It is also true that simvastatin has substantial LDL-lowering activity, and you might be able to reach your LDL goal with this drug as well. However, due to the tight link between LDL level and arterial blockage/associated heart disease, the more you can lower your LDL levels right now, the healthier you will be. Therefore, Crestor is a significantly more attractive drug as based on the criterion of LDL reduction.

(II). Secondary Effectiveness: Changes to Other Parameters

Introduction

In the previous section of the report, I discussed the ability of each drug to lower your LDL levels, since that should be their primary function in your regimen. However, a variety of other factors in the human body combine to affect the progression of atherosclerosis. While I know you have done significant reading about lowering LDL, you may not be as familiar with these other parameters, so let’s start off with some background information.

The HDL complexes in your bloodstream carry cholesterol back to the liver for degradation; thus, they are helping to reduce the amount of cholesterol in your system and are the “good” form of cholesterol. As mentioned previously, a low LDL/HDL ratio is favorable (12). An average adult male should have an HDL reading of about 40-50 mg/dL; your latest reading was 40 mg/dL, which is on the low end of the range (25). An increase to 45 mg/dL, or 12%, would be a reasonable goal for your drug/exercise/diet regimen. In general, exercise has been shown to have the greatest effect on HDL levels, since most current statins do not have much of an effect on HDL levels. Another important factor in the occurrence of further coronary disease is your apolipoprotein B level. Apolipoproteins are a part of the HDL and LDL complexes. High levels of apolipoprotein B (apo-B) are associated with decreased lipid recycling and an increase in atherosclerosis and frequency of heart attack (6). A reduction of apo-B levels should be of prime importance to you, since heart disease is a condition that runs in your family. It may be that you are genetically predisposed to high apo-B levels. If so, reducing apo-B could significantly decrease your risk of future heart attacks. Finally, one other factor in the development of coronary disease is the inflammation process in the coronary arteries. When inflammation is triggered, which can occur through stress, infection, or high levels of oxidants, neutrophils are stimulated to attach to your coronary arteries. These cells
then engulf cholesterol and become fatty plaques. Drugs that block steps of this inflammation process can help prevent the progression of atherosclerosis.

Therefore, an ideal drug candidate for you would significantly reduce apo-B levels and would have some impact on boosting HDL levels and blocking inflammation pathways. In this section of the report, I compare the effects of simvastatins and rosvastatins on HDL and apo-B levels and then examine their role in inflammation.

**HDL and Apolipoprotein Profile**

According to the package insert for Zocor, simvastatins can increase blood HDL levels by as much as 8% (27). Such an increase would help bring your HDL close to its target level. However, clinical trials which directly compared increases in HDL found that 5 and 10 mg doses of rosvastatin increased HDL levels 12 and 13% respectively, as compared to 20 mg does of simvastatin, which increased HDL levels 8% (10). Therefore, you could achieve your HDL goal with rosvastatin alone, but not with simvastatin alone. However, further studies need to be done to determine the role of rosvastatin on the overall HDL profile. Both simvastatin and atorvastatin, the statin found in Lipitor, are known to increase the percentage of the forms of HDL that recycle cholesterol effectively (2). In a separate clinical trial focused on LDL levels, rosvastatin was also found to increase HDL levels more than simvastatins, by a statistically significant margin (22).

One particularly critical aspect of the blood profile that has been investigated is the level of apo-B, as described above. Preliminary evidence of an effect on apo-B levels was presented by the LDL-focused clinical trial mentioned above. Rosuvastatin not only was better at increasing HDL levels, but it was also better at decreasing apo-B levels, by a statistically significant margin (6). In clinical trials conducted by AstraZeneca, 10 mg doses of rosvastatin reduced levels of apo-B an average of 42% (8). In contrast, I could not find a simvastatin study that lowered apo-B levels in patients more than 35.3%.

**Inflammation Response**

Even if you lower LDL and apo-B levels, high levels of inflammation along your coronary arteries could cause you to experience high levels of plaque buildup. Due to the older age of simvastatins, their role in blocking inflammation has been more comprehensively studied. In studies of human hearts, simvastatins have been shown to alter the proteins that are produced in the cells of the artery (11). As a result, the adherence of the plaque-causing neutrophils is negatively affected. The anti-inflammatory properties of simvastatin can be very powerful. One study examined the effect of the drug in hearts exposed to the alpha-toxin of *Staphylococcus aureus*, which causes significant inflammation and binding of neutrophils to the endothelium. If the hearts were pretreated with simvastatin, then there was a significant reduction in the amount of damage and plaque buildup in the heart (20). As a result, simvastatins may have anti-inflammatory properties that are separate from their cholesterol-lowering properties in reducing the risk of heart attack. Very recent studies in a mouse system
have indicated that rosuvastatins may play a similar role in reducing endothelial binding during stress (13, 14). Although this link has not yet been determined in humans, the authors of the mouse study expect that rosuvastatin will play an anti-inflammatory role as least as significant as that of simvastatin.

Conclusion

Rosuvastatins are not just superior to simvastatins in their ability to lower LDL levels; rosuvastatins also have an increased ability to elevate HDL levels, create more favorable lipid profiles in the blood, and decrease apo-B levels. Rosuvastatins could play a significant role in helping you reach your HDL cholesterol goal, whereas, with the simvastains, you would essentially have to reach your goal by diet and exercise alone. The apo-B reduction is good news if the genetic link to your coronary disease does involve apo-B levels (which, of course, we do not know for one way or the other). The link between simvastatin and anti-inflammatory properties is more convincing, but this discrepancy is most likely due to the differing amount of research that has been conducted on each statin. Therefore, rosuvastatins are also superior to simvastatins on the criterion of secondary effectiveness properties.

(III). Severity of Side Effects

Introduction

The possibility of further heart attacks and stroke, both of which are potentially lethal, has certainly been central on your mind. Therefore, you may not have thought very much about the potential side effects of these medications before beginning their use. However, in comparison to other drugs you have taken, such as antibacterials, antivirals, and antifungals, statins are not blocking a chemical reaction or biological process particular to an invading pathogen. Rather, they are blocking a cellular enzyme that carries out a common biochemical reaction that takes place in many of the cells of our body, especially the liver. Therefore, statins have the potential to cause serious harm to the body.

You certainly do not want to die or become seriously impaired from a drug you were taking to reduce the risk of future problems. Therefore, it is important to evaluate if either, or both, of these drugs poses the potential for serious side effects. In addition, any side effects that would reduce your mobility would be very undesirable. A one-hour walk is an important component of your current post-operative regimen. Therefore, any drug-induced condition that hampered your ability to move effectively could hurt your heart’s state of health more than it would help it.

From my own experience with taking prescription medicines, commercials, package inserts, and even doctors tend to downplay the number and severity of potential side effects. Therefore, in this section of the report, I compare the side effects of simvastatins and rosuvastatins to determine which one, if either, puts you at a greater risk for complications. No studies have been done that directly compare the effects of these
two drugs. As a result, first, I describe the potential side effects of simvastatins, and next, I describe the potential side effects of rosuvastatins.

Simvastatin Side Effects

Since the simvastatins have been on the market for several years, much is known about the frequency of their side effects. An investigation of the FDA database of all cases of reported adverse effects with simvastatins revealed only 210 cases of adverse events affecting major organ systems (such as the liver, pancreas, muscle, and bone marrow) per 1 million 10 mg doses of the drug (1). Therefore, each 10 mg dose only carries a 0.02% chance of a major side effect. Since you are taking a 20 mg dose, the frequency of effects would be slightly higher for you specifically. The most common serious side effect was muscle problems, or myalgias; the occurrence of muscle problems appears to be a trait shared by all of the statins on the market. Other potential organ effects include changes in the liver, pancreas, and bone marrow, all of which were rare compared to muscle problems. This database also indicated some occurrences of both rhabdomyolysis, which can be fatal, and a severe allergic syndrome. Since you have already started taking doses of Zocor with no immediate problems, it is unlikely that you would develop the allergic syndrome in the future. Rhabdomyolysis, on the other hand, which involves the release of toxic compounds from the muscle into the bloodstream, could potentially occur in the future. However, only a few of the 210 reported cases of major organ problems resulted in hospitalization and/or death. Therefore, while simvastatins carry the risk of some serious side effects, their relative safety over a long-term period (5 years) has been confirmed.

Rosuvastatin Side Effects

In contrast, rosuvastatin has just recently passed its clinical trials. No appreciable database exists for rosuvastatin patients, and no long-term information exists for the drug. Much of the information about its properties in the body is theoretical.

For example, the particular chemical side groups on rosuvastatin make it a hydrophilic molecule, as seen clearly in Fig. 1. Simvastatin, on the other hand, is hydrophobic, like most of the other statins (7). This hydrophilicity makes rosuvastatin selective for entering hepatic cells (18). This is a beneficial property since the specific organ where cholesterol synthesis by HMG Co-A reductase occurs is the liver. Instead of penetrating and interfering with many different kinds of cells in the body like the hydrophobic simvastatin, rosuvastatin can limit its effect to its target cells.
Another favorable chemical property is the way rosvastatin is metabolized. It is broken down inside your cells by a protein called cytochrome P450, as opposed to all other statins, which are broken down by proteins known as 2C9 and 2C19 (17). Breakdown by cytochrome P450 makes rosvastatin less likely to cause drug interactions. Right now, you are not taking any other prescription medicines. However, if you were to develop a bacterial infection such as bronchitis or pneumonia, both of which are typical in the winter, you might need to take an antibiotic. Two commonly prescribed antibiotics, erythromycin and clarithromycin, have adverse drug interactions with simvastatin, but not with rosvastatin (8). It might be possible for you to use another type of antibiotic, but since antibiotic-resistant strains of bacteria are increasing in prevalence in the human population, it is possible that you would need to take one of these two antibiotics. It is important to keep in mind, however, that it can be very difficult to predict the type of effect a drug will have in the body until you actually conduct extensive trials; therefore, these theoretical assumptions should be viewed with caution. One downside to rosvastatin is its unusual interaction with some antacids. Certain antacid formulations lead to a decrease in serum levels of the drug, which could decrease its efficacy (8). I know that you take antacid tablets relatively frequently, so you would need to examine your antacid selection carefully if on Crestor.

In addition to the theoretical chemical properties of rosvastatins, there is some evidence from clinical trials to indicate their safety. In a one-year clinical trial comparing simvastatin and rosvastatin, doses up to 80 mg/dL of both simvastatin and rosvastatin were well tolerated in all 477 patients (5). In a 12-week study comparing rosvastatin and atorvastatin (brand name-Lipitor), no significant adverse effects were exhibited by any of the rosvastatin patients (10). In contrast, 3.9% of the atorvastatin patients experienced adverse effects. Since this trial did not involve simvastatin, no direct comparisons can be made; however, simvastatin and atorvastatin are known to have very similar frequencies of side effects (1). In my literature search of clinical trials published in medical journals, I did not find any studies in which rosvastatin caused any severe
effects. However, the patient information for Crestor warns against the occurrence of myalgias and other muscle problems (8). Therefore, based on the current information, rosuvastatin has fewer short-term side effects than simvastatin.

<table>
<thead>
<tr>
<th>Table 1: Comparison of Minor Side Effects</th>
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<tr>
<td><strong>Type of Side Effect</strong></td>
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<td>-------------------------</td>
</tr>
<tr>
<td>Constipation</td>
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<tr>
<td>Flatulence</td>
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<td>Nausea</td>
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<td>Myalgia</td>
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Relative ratios were obtained by dividing percent incidence of condition in drug group by percent incidence of condition in placebo group. Results were obtained from two different studies due to the lack of a direct comparison study. Doses were 10 mg rosuvastatin and 20 mg simvastatin. From refs. (27) and (10).

This does not mean that rosuvastatin is free of side effects, however. The aforementioned clinical trial with 132 patients, rates of constipation, nausea, flatulence, and myalgia were monitored as compared to a group that had simply taken a placebo pill. All reported side effects occurred in less than 4% of patients. Again, unfortunately, the data compares rosuvastatin to atorvastatin and not simvastatin; no direct comparisons are available in the literature. In Table 1, however, I have combined the results from two separate studies. I calculated a risk ratio for each condition by dividing the percent incidence in the drug group by the percent incidence in the placebo group. Both drugs exhibit only mild, if any, side effects in most patients in the short-term. Therefore, neither drug would be expected to impact your daily exercise negatively.

**Conclusion**

Both rosuvastatin and simvastatin appear to be well-tolerated drugs. The chemical properties of rosuvastatin suggest that it has the potential to have far fewer side effects than other classes of statins, including the simvastatins. However, while the safety of simvastatin has been demonstrated over a period of over 5 years, the long-term effects of rosuvastatin are still to be determined. Recently, a different statin, cerivastatin, was pulled off the market due to its high rate of fatal rhabdomyolysis over time (24). A similar situation could arise for rosuvastatin. Based on the preliminary nature of rosuvastatin safety tests, simvastatin would be a better choice at the present based on the criterion of safety. It is important to keep in mind, though, that even if rosuvastatin was shown to have a high incidence of a condition like rhabdomyolysis, most people taking the drug will never develop this condition. The risk-benefit ratio of every statin is very high, since they are helping to prevent fatal conditions.
(IV). Practicality of Use

Introduction

Now that we have examined the effectiveness and the side effects of each drug, we have reached our final point of comparison—how practical would it be to integrate each type of drug into your daily life? Your doctors have told you that the results of a coronary bypass operation can last as long as 10 years, or even longer. For that to occur, however, you will need to continue your cholesterol-lowering regimen. Therefore, you will most likely be taking a statin for the rest of your life. If taking your statin is now a part of your daily life, purchasing and consuming the medication should be as little of a burden as possible. For example, you should not be paying exorbitant fees for monthly doses of your medicine. In addition, you want a drug that can be adjusted depending on your needs. If you are not meeting your cholesterol goals with your initial dosage, an ideal drug would allow you to change the dosage until you do find a level that will be effective. This is especially true for your particular situation, since you are looking to reduce already relatively low cholesterol levels even further. Therefore, you may need higher drug dosages to achieve these goals. Currently, your doctor has prescribed 20 mg/dL of Zocor as an initial dosage. In this final section of the report, I will first examine the predicted cost of use of each type of drug; next, I will examine the ease with which the pills can be obtained and ingested; and finally, I will consider the flexibility of dosage of each drug.

Cost of Use

You doctor informed you that one of the main reasons you are taking Zocor over other drugs, including the #1 prescribed drug Lipitor, is the fact that your HMO supports the sale of Zocor. Since it is the recommended cholesterol-lowering drug for your HMO, you have to pay only ½ of the price of each bottle. A bottle of thirty 20 mg/dL dose tablets of Zocor provides a month’s supply, since dosage is 1 pill per day (27). Normally, this bottle would be $118, but, according to your last medical bill, your bottle of Zocor cost you only $59. Therefore, you would be spending $708 dollars a year. This is actually not a huge sum, since you are financially stable and this drug is presumably helping to save your life. If a bypass surgery generally lasts about 10 years before another one must be redone, then the cost of Zocor is about $7,000 between surgeries.

Since Crestor is not available in the United States, its price information is not yet known. However, we can make speculations as to how the future price of Crestor will compare to the current price of Zocor. First, the drug has already been released in both Canada and Europe, and it is currently sold at a price of 0.78 euros per 10 mg dose (9). We will assume that you would start on the 10 mg dose of Crestor, which is typical for heart patients. Based on the current conversion rate of approximately 1.087 euros to the dollar, each dose would cost you $0.71, so the cost of a 10 mg Crestor regimen is only $21 monthly, or $258 yearly. However, the conditions of a U.S. market will be different. In the Dutch market, the prices of all statins are cheaper, and Crestor prices are similar to the prices of other statins, like Lipitor (9). It is likely that Crestor would also be sold in
the U.S. at a price similar to U.S. statin prices. Since you would be taking less mg of Crestor than Zocor, that would decrease your yearly cost, but, since the HMO only pays for Zocor right now, using an unrecommended drug would increase the cost. Therefore, we cannot predict exactly how much Crestor will cost when it hits the U.S. market, but, based on the European market, it will not be an example of an exorbitantly priced new drug. Even without payment by the HMO, Crestor may not be any more expensive to take than Zocor, and may even be cheaper.

Ease of Use

On a basic dosage level, the ease of use of both medications is approximately the same. Both Crestor and Zocor are administered orally by taking a pill once daily (8, 27). However, one benefit to Crestor is that it can be taken either morning or night, whereas Zocor must be taken at night (16). I know you are much more of a morning person, so Crestor would allow you to switch your dosage schedule to fit your preferred daily schedule. However, since it takes less than a minute to swallow the pill, this consideration is not a major concern.

What is a significant concern, on the other hand, is the fact that Crestor is not currently available in the U.S. While most sources expect it to be released to pharmacies very soon, there can be no guarantees. Once it is released, you will not just be able to grab it off a shelf at the local pharmacy. You will have started on your Zocor prescription, and you would need an entirely new prescription from your doctor to switch to Crestor. If your doctor is wary of new drugs, he may not want to have you switch medicines, or, if he sees that you have exhibited a decrease in blood cholesterol levels already, he may not deem the switch necessary. Plus, since you will have already started the Zocor regimen when Crestor comes out, you may feel more comfortable with the Zocor pills. You will be used to taking the Zocor pills and (most probably) will not have suffered any side effects. Therefore, you might be personally resistant to change once you begin the medicine.

(V). Flexibility of Use

The last factor for consideration is the flexibility of dosage for each drug. For Zocor, current dosages are 10 and 20 mg, with a 20 mg dosage being more common (27). I found very few clinical studies that examined patients with simvastatin dosages higher than 20 mg/dL, which may be due to the increase in side effects. On the other hand, an introductory dosage of Crestor is 5 mg, which can be increased to 10 mg if there is not sufficient improvement in cholesterol levels (8). A 5 mg dose of Crestor can drop LDL levels more than your current 20 mg/dL dose of Zocor; therefore, Crestor is a more potent statin than Zocor (4, 19). There is a physical reason behind the difference in potency between the drugs-- their differing binding properties. Rosuvastatin simply binds and inhibits the active site of HMG CoA-reductase more tightly than simvastatin (17).
Why is a more potent statin useful to you? First, the risk of conditions like myalgia and rhabdomyolysis increases with the size of the statin dose (27). The less statin you take, the fewer problems you would be expected to have. Also, if you do not reach your cholesterol goals with the 20 mg/dL dose of Zocor, your doctor could not increase your dose very much. With Crestor, in comparison, your doctor could easily increase your dose from 5 to 10 mg, or even to 20 mg, to improve your cholesterol-blocking potential. If you do increase your dose of Crestor, AstraZeneca trials of rosuvastatin demonstrated that levels of LDL and non-HDL cholesterol both decreased in a dose-dependent manner (8). I did not find any evidence for a similar, strong-dose response for simvastatin. Therefore, Crestor offers a greater possibility of reaching a dose that will be effective at lowering your cholesterol levels.

Conclusion

The main disadvantage of Crestor has been obvious from the very beginning of this report—it is simply not available yet in the U.S., and thus you will not be able to start taking this drug immediately. However, all other basic characteristics of Crestor make it as suitable or more suitable than Zocor for practical use. Of greatest benefit is Crestor’s flexibility of dosage and its strong dose-response effect. While you may be able to attain your cholesterol goals with your starting doses of Zocor, Crestor provides more options if your cholesterol levels are not dropping like they should. Also, since Crestor contains a higher potency statin, it has the potential to be cheaper and to cause fewer side effects. Therefore, once Crestor enters the market, it will be the superior statin on the criterion of practicality of use.

CONCLUSIONS

Based on the comparison of the effectiveness and the side effects of simvastatin (brand name-Zocor®) and rosuvastatin (brand name-Crestor®), a rosuvastatin is a better choice for your cholesterol-lowering regimen. Rosuvastatins are superior to simvastatins in the improvement of your target areas—reduction of LDL and apo-B levels, and an increase in your HDL levels. While the long-term side effects of rosuvastatin are not known, the incidence of serious side effects during medication with other statins is generally quite low. Since you are faced with a potentially life-threatening condition, the potential benefits of rosuvastatin far outweigh the safety risks. Also, the increase in benefits from simvastatin to rosuvastatin outweighs any potential differences in safety between the two drugs. Therefore, if you had to select the drug today, and both were available, the decision would be very clear.

Since the drug Crestor is not currently available, however, the situation is more complex. If you begin Zocor and have positive results, should you go through the hassle of switching drugs? In your situation, the answer is yes. The lower your LDL levels, the better the chance that you will avoid a heart attack or a stroke. Reaching your cholesterol target cannot guarantee that you will have no problems in the future.
Surprisingly, you may be able to obtain this more effective drug just as cheaply as you could Zocor. In the event that the price of Crestor is significantly more expensive than Zocor, I still recommend an immediate switch. Your health and longevity are worth more than what any sum of money can buy. Also, by reducing your LDL levels now, you will avoid the need for expensive surgery and emergency room bills in the future. It is possible that your main obstacle might be your doctor, who could be resistant to you changing drug types immediately. I suggest that you supply him with a copy of this recommendation report on your next visit to convince him of the need for Crestor in your life. As Crestor increases in popularity, it is possible that your HMO will select it as a part of its prescription drug plan, which could reduce the amount of money you will have to spend on Crestor even further.

Since Zocor is your only choice right now, you have no alternative but to begin this regimen, and this medication should have some positive effect on your blood cholesterol levels. Then, after Crestor is approved, you can switch drugs and hopefully experience an even further reduction in your blood cholesterol levels. Remember, though, to continue with your exercise and diet regimen. A healthy diet and exercise plan have many more benefits to the cardiovascular system than any drug could have.

RECOMMENDATIONS

--Therefore, I suggest that you take the following steps in the future:

✓ Begin the Zocor pill regimen

✓ Sign up on the Crestor web page, http://www.crestor.com, to receive an email update whenever the medication becomes available in the United States

✓ Schedule an appointment with your cardiologist and bring him a copy of this report

✓ Ask your doctor to switch to a 10 mg/dL dose of Crestor, the rosuvastatin

✓ Take your Crestor pill every morning

✓ Continue with your diet and exercise plan as before

✓ Receive frequent blood cholesterol tests to monitor your progress

✓ Receive at least semiyearly liver tests to check for an adverse reaction

✓ Live a long, happy, heart-healthy life! ❤
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