Treating to Meet NCEP-Recommended LDL Cholesterol Concentrations with Atorvastatin, Fluvastatin, Lovastatin, or Simvastatin in Patients with Risk Factors for Coronary Heart Disease

Donald Hunninghake, MD; Rebecca G. Bakker-Arkema, MS; James P. Wigand, MD; Margaret Drehobl, MD; Helmut Schrott, MD; James L. Early, MD; Paul Abdallah, MD; Scott McBride, MA; and Donald M. Black, MD
Minneapolis, Minnesota; Ann Arbor, Michigan; Richmond, Virginia; San Diego, California; Iowa City, Iowa; Wichita, Kansas; and Seattle, Washington

BACKGROUND. Our study compared use of atorvastatin, fluvastatin, lovastatin, and simvastatin for lowering low-density lipoprotein (LDL) cholesterol concentration in patients at risk for coronary heart disease (CHD). The goal was to reach the LDL cholesterol levels recommended by the National Cholesterol Education Program (NCEP).

METHODS. A combined total of 344 men and women took part in this 54-week, multicenter, open-label, randomized, parallel-group, active-controlled, treat-to-target study. Patients were selected on the basis of their LDL cholesterol concentration and their risk for CHD. During treatment, doses were titrated at 12-week intervals to a maximum of 80 mg per day of atorvastatin and lovastatin, or 40 mg per day of fluvastatin and simvastatin, with colestipol added if necessary to attain the NCEP-recommended LDL cholesterol concentration.

RESULTS. At the starting dose, atorvastatin decreased plasma LDL cholesterol significantly ($P < .05$) compared with the other reductase inhibitors, and the percentage of patients reaching target LDL cholesterol concentration at the starting dose was significantly greater in the atorvastatin group ($P < .05$). Overall, a significantly ($P < .05$) greater percentage (95%) of atorvastatin-treated patients achieved target LDL cholesterol concentration. The safety profile was similar among all reductase inhibitors tested.

CONCLUSIONS. At the starting dose, a significantly ($P < .05$) greater percentage of atorvastatin-treated patients at risk for CHD reached the target LDL cholesterol concentration than patients treated with other reductase inhibitors.

KEY WORDS. Cholesterol; atherosclerosis; coronary heart disease. *(J Fam Pract 1998; 47:349-356)*

Several clinical trials have demonstrated that elevated serum low-density lipoprotein (LDL) cholesterol is associated with increased risk of coronary heart disease (CHD), and that lowering serum LDL cholesterol levels reduces the likelihood of new coronary events and associated mortality.[1-2] In 1993, the Adult Treatment Panel (ATP-II) report of the National Cholesterol Education Program (NCEP) outlined an updated systematic clinical approach to treating high blood cholesterol in adults.[3] These NCEP guidelines are based on the patient's existing LDL cholesterol concentration and risk for CHD. The expert panel recommends lipid-lowering drug treatment if, after an attempt at dietary intervention, LDL cholesterol remains ≥190 mg/dL in patients with less than 2 CHD risk factors or ≥160 mg/dL in patients with 2 or more CHD risk factors.

Atorvastatin is a new 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitor that has been shown to lower LDL cholesterol 41% to 60% over its effective dose range.[4-6] In our study, we prospectively evaluated the ability of atorvastatin to treat patients at risk for CHD to their NCEP-recommended target LDL cholesterol concentration. Atorvastatin was compared with three frequently prescribed reductase inhibitors: fluvastatin, lovastatin, and simvastatin. Our study is the first direct comparison between these agents in a dyslipidemic population being treated to NCEP-recommended LDL cholesterol concentrations.

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From the University of Minnesota (D.H.); Wigand, Wasserman, Burris & Young Medical Associates (J.P.W.); Center for Health Care Medical Associates (M.D.); University of Iowa (H.S.); University of Kansas School of Medicine (J.L.E.); Minor & James Medical (P.A.); and Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Co (R.G.B., S.M., D.M.B.). Requests for reprints should be addressed to Rebecca G. Bakker-Arkema, Parke-Davis Pharmaceutical Research, 2800 Plymouth Rd, Ann Arbor, MI 48105-1047.

METHODS

Study Design

This 54-week, open-label, randomized, parallel-group, active-controlled, treat-to-target study in patients at risk for cardiovascular disease consisted of three phases: an optional 8-week screening and dietary assessment phase, a 4-week lead-in phase, and a 54-week open-label treatment phase. The study ran from March 1995 to October 1996. We recruited patients from 24 facilities reflecting a broad range of medical practices in the United States, including 12 primary (eg, internal medicine, family practice) and 12 secondary (eg, cardiology, lipid) centers. Identical protocols were reviewed and approved by an institutional review board. Patients gave written informed consent before participating. Women of nonchildbearing potential, and men and women at risk for CHD, aged 18 to 80 years, and with a body mass index ≤32 kg/m^2 were screened for eligibility with a physical examination, a medical history, a clinical laboratory evaluation, a urinalysis, and a lipid profile. Eligible patients were required to adhere to the NCEP Step I or Step II diet or a similar diet during the study.[3,7] We allowed the lipid levels of patients beginning dietary modification to stabilize over an 8-week period before the patient entered the 4-week lead-in phase (see Figure 1). The lead-in phase was used to further evaluate the patient's eligibility and to establish baseline values for study parameters. Fasting triglyceride values of ≤400 mg/dL were necessary for inclusion. Patients were also grouped according to their number of risk factors as described by the NCEP: less than 2 risk factors for CHD and mean cholesterol ≥190 mg/dL or 2 or more CHD risk factors and a mean LDL cholesterol value of ≥160mg/dL. Mean LDL was calculated using the Friedewald formula at weeks -4 and -2.[8] A total of 344 patients were randomized to the study: 82 with fewer than 2 risk factors and 262 with 2 or more risk factors. The distribution of patients within risk categories was similar across treatment groups. Patient exclusions are listed in Table 1.

TABLE 1

Exclusion Criteria for Study Comparing Atorvastatin, Fluvastatin, Lovastatin, and Simvastatin

- Hypersensitivities to reductase inhibitors or bile acid sequestering resins
- Prohibited medications, such as lipid regulating drugs not prescribed in the protocol, immunosuppressive agents, and drugs known to be associated with rhabdomyolysis in combination with reductase inhibitors (ie, cyclosporine, erythromycin)
- Pregnancy or breast-feeding
- Secondary causes of hyperlipoproteinemia, such as uncontrolled hypothyroidism, nephrotic syndrome, severe renal dysfunction, or uncontrolled type 1 or type 2 diabetes mellitus
- Active liver disease or hepatic dysfunction
- Myocardial infarction, coronary angioplasty, coronary artery bypass graft, or severe or unstable angina pectoris within 1 month of screening
- Participation in another clinical study in which study medication was received within 30 days of screening for this study
- Significant abnormalities that the investigator judged could compromise the patient's safety or successful participation in the study

Eligible patients were randomized to 1 of 4 treatment groups using starting doses of atorvastatin 10 mg per day, fluvastatin 20 mg per day, lovastatin 20 mg per day, or simvastatin 10 mg per day. Lipids were measured at 6-week intervals, and dose titration occurred at 12-week intervals (weeks 12, 24, 36 and 48), until the patient reached the LDL cholesterol concentration recommended by the NCEP ATP-II.

The dose of reductase inhibitor could be increased to a maximum of 80 mg per day for atorvastatin, 40 mg per day for fluvastatin, 80 mg per day for lovastatin, and 40 mg per day for simvastatin (the maximum approved dose at the time of the study). If target LDL cholesterol concentration was not achieved at the maximum dose of the reductase inhibitor, colestipol was added to the patient's regimen, initially at 5 g twice daily. On the basis of the patient's response, the colestipol dose could be increased by 5 g twice daily after a 12-week interval, to a maximum of 20 g per day. If the patient could not tolerate the drug, the dose could be decreased or totally withheld.

Once the target LDL cholesterol concentration was reached, the patient's dose of mono- or combination-therapy was maintained with no further titrations regardless of subsequent LDL cholesterol values. Lipids were measured at 12-week intervals until the end of the study. At weeks 0 and 54, patients completed a 24-hour dietary diary. An investigator reviewed the contents of the diaries for completeness and sent them to the Chicago Center for Clinical Research, where a food record rating score was calculated.[9] Noncompliant patients (those who took less than 80% of their prescribed medication) were counseled but were not dropped from the study.

Efficacy and Safety Measurements

Clinical and safety evaluations and lipid profiles were managed through an accredited, standardized, central laboratory (Pacific Biometrics Research Foundation, Seattle, Washington). Serum samples for lipid profiles were collected after a minimum 12-hour fast, and blood samples for lipid profiles were drawn between 6 and 18 hours postdose.

We evaluated total cholesterol, LDL cholesterol, triglyceride, and high-density lipoprotein (HDL) cholesterol levels. Triglyceride levels were determined enzymatically with the Hitachi 737 analyzer.[10] Plasma HDL

cholesterol concentration was determined enzymatically after LDL and very-low-density lipoprotein (VLDL) cholesterol were selectively removed from the plasma sample by heparin and magnesium chloride precipitation.[11] For triglyceride levels <400 mg/dL,[8] LDL cholesterol concentration was estimated using the Friedewald formula. For triglycerides ≥400 mg/dL, LDL cholesterol levels were determined by ultracentrifugation.[12]

A full clinical laboratory evaluation was performed at screening, at randomization, and at the end of the study, while evaluations for safety (alanine aminotransferase [ALT], aspartate aminotransferase [AST], and creatine phosphokinase [CPK]) were done at all intervening visits. Adverse events were recorded at each clinic visit and up to 15 days after treatment ended. Associated adverse events were those the investigator judged as definitely, probably, or possibly related to treatment, as well as those that had an unknown relationship to treatment or insufficient information available for evaluation.

STATISTICS

Power The sample size calculation was based on a two-sided *t* test at the 5% level of significance. Patients were stratified by CHD risk factors so that patients with 2 or more CHD risk factors were 75% of the total sample and patients with less than 2 CHD risk factors were 25% of the total sample. The percentage of patients reaching target at each visit was estimated. The estimate of the mean number of visits needed to reach target in each treatment group yielded a difference of 1.5 between atorvastatin and simvastatin. An estimate of 3.0 for the standard deviation was used for determining sample size. A sample of 68 patients per group would detect a difference of 1.5 visits with 80% power. Estimating a 15% dropout rate yielded a requirement of approximately 80 patients per group.

Efficacy Descriptive statistics were prepared for all baseline demographic and lipid variables. Statistical tests were performed on data from weeks 12 (starting dose), 24 (before colestipol adjuvant therapy), and 54 (end of study). Efficacy analyses were performed on data from an intent-to-treat population, defined as all patients who received at least one dose of study medication and who had at least one lipid measurement taken after randomization. All statistical tests were two-sided and conducted at the 5% level of significance.

Analysis of covariance was performed to compare the effects of the 4 treatments on the percent change from baseline in LDL cholesterol levels, total cholesterol, triglycerides, and HDL cholesterol, at weeks 12, 24, and 54. The model included the effects of treatment, center, CHD risk factors, and the baseline lipid value as a covariate. A Dunnett test was used to perform pairwise comparisons between atorvastatin and the other treatments. The last available postrandomization lipid measurement was carried forward to explain missing observations.

For determining the percentage of patients reaching target LDL cholesterol concentration, responders were those patients with less than 2 CHD risk factors whose mean LDL cholesterol was <160 mg/dL or patients with 2 or more CHD risk factors whose mean LDL cholesterol was <130 mg/dL. Patients were counted as responders at weeks 12, 24, and 54 if they had achieved that status at

FIGURE 1

Study Design

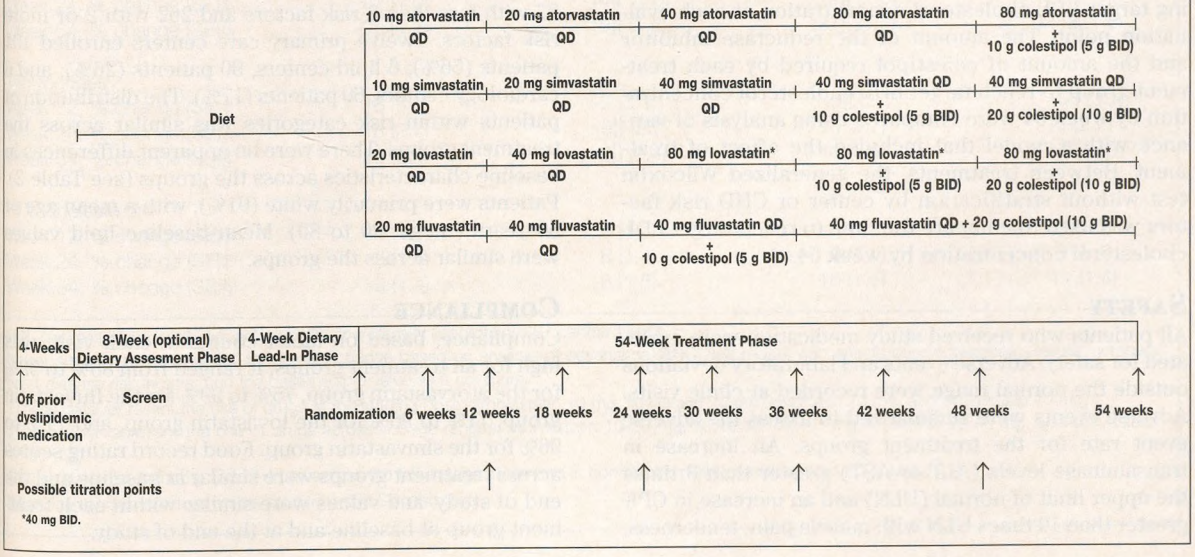


TABLE 2

Baseline Patient Characteristics

Characteristic	Atorvastatin (n = 86)	Fluvastatin (n = 85)	Lovastatin (n = 86)	Simvastatin (n = 87)	All Patients (N = 344)
Sex, no. (%)					
Men	40 (47)	34 (40)	46 (53)	41 (47)	161 (47)
Women	46 (53)	51 (60)	40 (47)	46 (53)	183 (53)
Race, no. (%)					
White	80 (93)	75 (88)	76 (88)	81 (93)	312 (91)
Other	6 (7)	10 (12)	10 (12)	6 (7)	32 (9)
Age, years					
Median	55	55	55	58	56
Range	20 to 80	28 to 77	27 to 78	27 to 78	20 to 80
Mean (SE)	55 (1.4)	56 (1.3)	55 (1.2)	57 (1.3)	56 (0.6)
CHD risk factors, no. (%)					
<2	22 (26)	21 (25)	20 (23)	19 (22)	82 (24)
≥2	64 (74)	64 (75)	66 (77)	68 (78)	262 (76)
Lipid values (mg/dL), mean (SE)					
LDL-C	205 (4.3)	201 (4.1)	206 (3.9)	210 (5.5)	205 (2.3)
Total cholesterol	286 (4.6)	286 (3.9)	290 (4.4)	292 (5.8)	289 (2.4)
Total TG	190 (7.4)	209 (8.8)	205 (8.2)	201 (8.4)	201 (4.1)
HDL-C	42 (1.2)	43 (1.1)	43 (1.2)	42 (1.0)	43 (0.6)

CHD denotes coronary heart disease; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglycerides.

the evaluation visit or at any previous titration visit, regardless of whether that status had been maintained throughout the study. All patients who withdrew without having met responder status were counted as nonresponders.

We used the Cochran-Mantel-Haenszel analysis stratified by center and CHD risk factors to compare the percentage of patients in treatment groups achieving target LDL cholesterol concentration at each evaluation point. The amount of the reductase inhibitor and the amount of colestipol required by each treatment group to reach target LDL cholesterol concentration by week 54 were compared using analysis of variance with a model that included the effect of treatment. Between treatments, the generalized Wilcoxon test without stratification by center or CHD risk factors was used to compare the time to reach target LDL cholesterol concentration by week 54.

Safety

All patients who received study medication were evaluated for safety. Adverse events and laboratory deviations outside the normal range were recorded at clinic visits. Adverse events were summarized to assess the adverse event rate for the treatment groups. An increase in transaminase levels (ALT or AST) greater than 3 times the upper limit of normal (ULN) and an increase in CPK greater than 10 times ULN with muscle pain, tenderness, or weakness were considered important laboratory deviations because of the increased incidence of these laboratory events with reductase inhibitors.

RESULTS

Demographics

A total of 344 patients were randomized into the study; 82 with less than 2 risk factors and 262 with 2 or more risk factors. Twelve primary care centers enrolled 194 patients (56%); 6 lipid centers, 90 patients (26%); and 6 cardiology centers, 60 patients (17%). The distribution of patients within risk categories was similar across the treatment groups. There were no apparent differences in baseline characteristics across the groups (see Table 2). Patients were primarily white (91%), with a mean age of 56 years (range: 20 to 80). Mean baseline lipid values were similar across the groups.

Compliance

Compliance, based on tablet counts at each visit, was high for all treatment groups. It ranged from 86% to 99% for the atorvastatin group, 75% to 99% for the fluvastatin group, 71% to 96% for the lovastatin group, and 71% to 96% for the simvastatin group. Food record rating scores across treatment groups were similar at baseline and the end of study, and values were similar within each treatment group at baseline and at the end of study.

Disposition and Exposure

Ninety percent of patients in the atorvastatin group completed the study compared with 88% for fluvastatin, 83% for lovastatin, and 89% for simvastatin. At the end of the study, 70% of atorvastatin patients were exposed to a maximum dose of 10 mg, and only 2% were exposed to combination therapy. In contrast, 20% of fluvastatin patients were exposed to a maximum dose of 20 mg, and 67% were exposed to combination therapy; 40% of lovastatin patients were exposed to a maximum dose of 20 mg, and 24% were exposed to combination therapy; and 43% of simvastatin patients were exposed to a maximum dose of 10 mg, and 24% were exposed to combination therapy.

Efficacy

Efficacy data are summarized in Table 3. Statistical evaluation of week 12 data and week 24 data indicated that atorvastatin decreased LDL cholesterol and total cholesterol levels to a significantly greater extent than fluvastatin, lovastatin, or simvastatin. HDL cholesterol concentration increased to a similar extent across all treatment groups.

At week 54, atorvastatin significantly lowered LDL cholesterol levels from baseline to a greater extent than fluvastatin and lovastatin, as monotherapy or in combination with colestipol. Atorvastatin-treated patients had significantly greater reductions in total cholesterol levels than fluvastatin-, lovastatin-, or simvastatin-treated patients. HDL cholesterol levels increased similarly across all treatment groups.

NCEP Target LDL Cholesterol Concentration

After 12 weeks of treatment, when all patients were given the starting dose of treatment, a significantly (P <.05) greater percentage of atorvastatin-treated patients (71%) achieved the target LDL cholesterol concentration compared with 16%, 34%, and 41% for fluvastatin-, lovastatin-, and simvastatin-treated patients, respectively. Results were similar at week 24. By the end of the study, the percentage of patients reaching the target LDL cholesterol concentration remained significantly (P <.05) higher for atorvastatin-treated (95%), than fluvastatin-treated (60%), lovastatin-treated (77%), or simvastatin-treated (83%) patients. Cumulative response

TABLE 3

Mean Percent Change* from Baseline in Lipid Parameters

Lipid Parameter	Atorvastatin (n = 85)	Fluvastatin (n = 82)	Lovastatin (n = 83)	Simvastatin (n = 87)
LDL cholesterol				
Week 12, % change (SE)†	-36 (1.3)	-14‖ (1.3)	-23‖ (1.3)	-29‖ (1.3)
Week 24, % change (SE)‡	-35 (1.3)	-19‖ (1.4)	-24‖ (1.4)	-29‖ (1.3)
Week 54, % change (SE)§	-36 (1.6)	-22‖ (1.6)	-28‖ (1.6)	-33 (1.6)
Total cholesterol				
Week 12, % change (SE)†	-28 (1.0)	-11‖ (1.0)	-17‖ (1.0)	-21‖ (1.0)
Week 24, % change (SE)‡	-27 (1.0)	-14‖ (1.0)	-18‖ (1.0)	-21‖ (1.0)
Week 54, % change (SE)§	-28 (1.2)	-15‖ (1.2)	-21‖ (1.2)	-24‖ (1.2)
Triglycerides				
Week 12, % change (SE)†	-16 (3.1)	-7 (3.1)	-5‖ (3.1)	-5‖ (3.1)
Week 24, % change (SE)‡	-18 (2.7)	-9‖ (2.7)	-13 (2.7)	-15 (2.7)
Week 54, % change (SE)§	-20 (3.4)	2‖ (3.4)	-16 (3.4)	-11 (3.4)
HDL cholesterol				
Week 12, % change (SE)†	4 (1.3)	5 (1.3)	5 (1.3)	6 (1.3)
Week 24, % change (SE)‡	5 (1.4)	8 (1.4)	9 (1.4)	9 (1.4)
Week 54, % change (SE)§	9 (1.4)	6 (1.5)	10 (1.5)	11 (1.4)

HDL denotes high-density lipoprotein; LDL, low-density lipoprotein; SE, standard error.

*Least squares mean provided for percent change based on analysis of covariance (ANCOVA) model with effects due to treatment, center, coronary heart disease risk factors, and the baseline lipid value as a covariate.

†These data represent the use of drugs at the starting dose: atorvastatin 10 mg, fluvastatin 20 mg, lovastatin 20 mg, and simvastatin 10 mg.

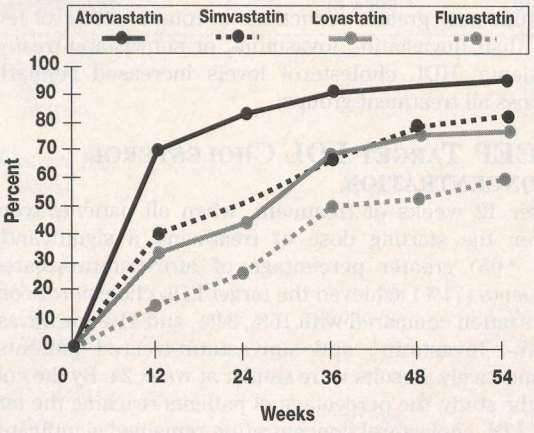
‡These data represent the use of drugs across dosage ranges: atorvastatin 10-20 mg, fluvastatin 20-40 mg, lovastatin 20-40 mg, and simvastatin 10-20 mg.

§These data represent the use of drugs across the full dosage range and in combination with colestipol adjuvant therapy.

‖Significantly different from atorvastatin (P <.05); Dunnett test.

FIGURE 2

Cumulative percentage of patients reaching the NCEP-recommended LDL cholesterol concentration.*



*Note: The median dose for each treatment group at week 54 (with the last available dose carried forward) was atorvastatin 10 mg per day, fluvastatin 40 mg per day, lovastatin 40 mg per day, and simvastatin 20 mg per day.

over time is shown in Figure 2.

Patients in the atorvastatin treatment group required significantly (P <.05) less time to reach the target LDL cholesterol concentration than patients in the other reductase inhibitor treatment groups. Atorvastatin-treated patients had a median time to response of 85 days compared with 269, 232, and 173 days for fluvastatin, lovastatin, and simvastatin, respectively.[13] Overall, target LDL cholesterol concentration was achieved in the atorvastatin treatment group with significantly (P <.05) less reductase inhibitor and with significantly (P <.05) less colestipol combination therapy than required in the other treatment groups.

The percentage of patients experiencing adverse events was similar for all treatments. Related adverse events were summarized at weeks 24 and 54. Week 24 was the last visit at which all patients were still taking monotherapy. Thus, adverse event summaries through 24 weeks were used to compare profiles between treatment groups without confounding effects from colestipol. Daily dose ranges at week 24 were 10 to 20 mg for atorvastatin, 20 to 40 mg for fluvastatin, 20 to 40 mg for lovastatin, and 10 to 20 mg for simvastatin. Adverse events experienced by at least 2% of patients were similar at these doses with 12% of atorvastatin, 16% of fluvastatin, 13% of lovastatin, and 9% of simvastatin patients reporting related adverse events (Table 4).

At week 54, when patients may have received reductase inhibitors and colestipol, the percentage of treatment-related adverse events experienced by at least 2% of the test population was the lowest for the atorvastatin group (14%), which was about half of the percentages for the fluvastatin group (34%) and the lovastatin group (24%). The simvastatin group experienced slightly more related adverse events (18%) than the atorvastatin group. Digestive system events were the most frequently reported treatment-associated adverse events, occurring with a higher incidence among fluvastatin- and lovastatin-treated patients than those receiving the other reductase inhibitors. Treatment-associated adverse events led to the withdrawal of 3% of the patients treated with atorvastatin, 4% treated with fluvastatin, 8% treated with lovastatin, and 5% treated with simvastatin. One patient experienced a serious adverse event (acute pancreatitis) considered associated with treatment while taking fluvastatin. Two patients randomized to receive lovastatin treatment died during the study. The study investigator did not associate either of these deaths with the study drug.

Some minor sporadic elevations in ALT and AST were noted in all treatment groups. Changes in remaining parameters were not clinically meaningful and showed no treatment-associated trends. One lovastatin-treated patient experienced ALT values over 3 times ULN. The study medication was temporarily stopped and the ALT level returned to within normal range.

DISCUSSION

Three hundred forty-four patients were enrolled in 12 primary and 12 secondary care facilities participating in our study. The majority of patients were enrolled by the primary care and lipid centers, supporting the fact that many patients at risk for developing CHD are being treated at these facilities. In addition, although the cardiology centers were designated as secondary care facilities, their patient recruitment (approximately 50% of the other sites) reflected a reasonable primary care patient base.

Study patients taking atorvastatin achieved their NCEP-recommended target LDL cholesterol concentration more often than patients using the other reductase inhibitors, with fewer office visits and less combination therapy. Consequently, mean total cost of care to reach the target concentration was lowest with atorvastatin.[13]

The percentage of related adverse events reported by at least 2% remained relatively consistent from week 24 to week 54 for atorvastatin compared with an almost two-fold increase for fluvastatin and lovastatin. Differences in adverse events may be attributed to the addition of colestipol, since the primary increases in adverse events were related to the digestive system. While only 2 atorvastatin patients (2%) had been exposed to combination therapy by the end of the study, 57 fluvastatin patients (67%), 20 lovastatin patients (24%), and 21 simvastatin patients (24%) were given colestipol. In normal primary care situations, an increased incidence of related adverse events due to

TABLE 4

Related Adverse Events, by Body Systems, Experienced by at Least 2% of Patients

Adverse Event*	Atorvastatin (n = 86)	Fluvastatin (n = 85)	Lovastatin (n = 86)	Simvastatin (n = 87)
Week 24†				
Body as a whole, no. (%)				
Abdominal pain	2 (2)	0 (0)	2 (2)	0 (0)
Headache	2 (2)	0 (0)	0 (0)	1 (1)
Digestive system, no. (%)				
Dyspepsia	2 (2)	4 (5)	3 (3)	0 (0)
Constipation	1 (1)	2 (2)	0 (0)	1 (1)
Flatulence	0 (0)	2 (2)	1 (1)	1 (1)
Nervous system				
Insomnia, no. (%)	0 (0)	1 (1)	1 (1)	3 (3)
Any event, no. (%)	10 (12)	14 (16)	11 (13)	8 (9)
Week 54‡				
Body as a whole, no. (%)				
Abdominal pain	2 (2)	3 (4)	2 (2)	0 (0)
Headache	2 (2)	0 (0)	0 (0)	1 (1)
Digestive system, no. (%)				
Flatulence	1 (1)	4 (5)	3 (3)	2 (2)
Nausea	1 (1)	1 (1)	0 (0)	2 (2)
Constipation	2 (2)	8 (9)	4 (5)	3 (3)
Dyspepsia	2 (2)	6 (7)	6 (7)	0 (0)
Diarrhea	0 (0)	2 (2)	1 (1)	3 (3)
Rectal hemorrhage	0 (0)	2 (2)	0 (0)	0 (0)
Nervous system, no. (%)				
Insomnia	0 (0)	1 (1)	1 (1)	3 (3)
Somnolence	0 (0)	0 (0)	2 (2)	0 (0)
Any event, no. (%)	12 (14)	29 (34)	21 (24)	16 (18)

*Considered possibly, probably, or definitely related to treatment or insufficient information.
†Patients receiving monotherapy.
‡Patients may have added colestipol adjuvant therapy.

resins has resulted in high discontinuance rates,[14] largely because of the occurrence of adverse events. Similarly, large discontinuance rates have been reported for these agents from pharmacy prescription refill data obtained in the primary care setting.[15] A greater percentage of atorvastatin patients met NCEP-recommended target LDL cholesterol concentration with monotherapy resulting in fewer drug-related adverse events, a lower discontinuance rate, and a slightly higher compliance rate than with those treated with either fluvastatin, lovastatin, or simvastatin.

Other studies have shown that reducing LDL cholesterol significantly reduces incidence of cardiovascular events.[1-2] In the West of Scotland Coronary Prevention Study, a maximum dose of pravastatin (40 mg per day) reduced LDL cholesterol by 26% and significantly reduced the incidence of myocardial infarction and death from cardiovascular causes in a primary prevention population.[2] Several ongoing atorvastatin studies are designed to examine its effects on cardiovascular events. In our study, patients treated with atorvastatin achieved a 36% reduction in LDL cholesterol concentration at the starting dose of the drug, allowing more than 70% of patients to meet their NCEP-recommended LDL cholesterol goal at this dose. Overall, target LDL cholesterol concentration was met with less combination therapy and consequently fewer side effects than patients treated with other reductase inhibitors. The results of our study indicate that atorvastatin is a highly effective treatment for a population at risk for CHD.

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