Efficacy and safety of atorvastatin in hyperlipidemic, type 2 diabetic patients. A 34-week, multicenter, open-label study

Carlos A. Aguilar-Salinas a,*, Francisco J. Gómez-Pérez a, Carlos Posadas-Romero b, Cuauhtémoc Vázquez-Chávez c, Eduardo Meaney d, Alfonso Gulías-Herrero a, Luz E. Guillén a, Alma Alvarado Vega b, Enrique Mendoza Pérez b, Luis Eduardo Romero-Nava b, Rita Angélica Gómez-Díaz c, Saúl Salinas-Orozco c, Rafael Moguel d, Germán Novoa e

a Instituto Nacional de la Nutrición ‘Salvador Zubirán’ de la SSA (Secretaría de Salud), Mexico City, Mexico
b Instituto Nacional de Cardiología ‘Ignacio Chávez’ de la SSA, Mexico City, Mexico
c Hospital de Cardiología, Centro Médico Nacional Siglo XXI del IMSS (Instituto Mexicano del Seguro Social), Mexico City, Mexico
d Hospital 1° de Octubre del ISSSTE (Instituto de Seguridad y Servicios Sociales para los Trabajadores del Estado), Mexico
e Parke-Davis, Mexico

Received 22 March 1999; received in revised form 16 November 1999; accepted 13 December 1999

Abstract

Hyperlipidemia is common in type 2 diabetic patients and is an independent risk factor for cardiovascular disease. The aim of this trial was to evaluate the efficacy and safety of once-daily atorvastatin 10 – 80 mg for the treatment of hyperlipidemia in type 2 diabetics with plasma low-density lipoprotein cholesterol (LDL-C) levels exceeding 3.4 mmol/l (130 mg/dl). One hundred and two patients met the study criteria and received 10 mg/day atorvastatin. Patients who reached the target LDL-C level of ≤ 2.6 mmol/l (100 mg/dl) maintained the same dosage regimen until they had completed 16 weeks of treatment. Patients not reaching the target LDL-C underwent dose titration to atorvastatin 20, 40 and 80 mg/day at Weeks 4, 8 and 12, respectively. All 88 patients who completed the study attained target LDL-C levels and 52 (59%) of patients achieved the target goal at the starting dose of atorvastatin 10 mg/day. In this group the differences between baseline and post-treatment values for LDL-C were 4.3 ± 0.7 mmol/l (166 ± 26 mg/dl) versus 2.2 ± 0.4 mmol/l (87 ± 14 mg/dl) (P < 0.0001), respectively, a decrease of 47%. Similar trends were observed for total cholesterol, triglycerides, very low-density lipoprotein cholesterol and apolipoprotein B levels. The safety profile of atorvastatin in these patients was highly favorable and similar to those reported with other statins. Only one patient withdrew due to a possible drug-related adverse event. These data confirm the marked efficacy and safety of atorvastatin in type 2 diabetic patients with hyperlipidemia and the efficacy of atorvastatin 10 mg in helping patients attain their LDL-C goal. © 2000 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Atorvastatin; Type 2 diabetes mellitus; Hypercholesterolemia; Low-density lipoprotein cholesterol; Triglyceride

1. Introduction

Type 2 diabetes is frequently associated with elevations of plasma low-density lipoprotein cholesterol (LDL-C) and triglycerides, and reduced levels of high-density lipoprotein cholesterol (HDL-C) [1,2]. Although elevated levels of LDL-C are found with equal frequency in diabetic and non-diabetic patients, LDL particle composition is altered unfavourably in diabetics and is more likely to be atherogenic. These lipid abnormalities are recognized as major risk factors for the development of coronary heart disease (CHD) and underlie the 2–4-fold greater prevalence of CHD, cerebrovascular disease and peripheral vascular disease in diabetic compared with non-diabetic patients [3]. It has been estimated that 75–80% of deaths among the diabetic population are attributable to cardiovascular disease, particularly ischemic heart disease [4,5].
A number of measures are recommended for the treatment of hyperlipidemia associated with diabetes. These include improved glycemic control, diet and weight modification, and control of other CHD risk factors, such as smoking and alcohol intake. If non-pharmacological strategies are not sufficient to control the lipid abnormalities, introduction of drug therapy may be warranted. Agents that are used to treat hypercholesterolemia or hypertriglyceridemia in non-diabetic patient groups, such as niacin and bile acid sequestrants, may not be suitable in patients with type 2 diabetes due to the possibility of aggravation of hypertriglyceridemia and/or insulin resistance [6]. In diabetic patients, drugs of choice to reduce LDL-C are the hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins) (some statins also reduce triglyceride levels), because they are generally well tolerated and do not adversely affect glycemic control. Data from subgroup analyses in recent cholesterol-lowering clinical trials using statin therapy indicate that the benefits of cholesterol lowering are at least as great in diabetic as in non-diabetic groups [7,8].

The results of a recent study have suggested that diabetic patients without CHD have as high a risk of a myocardial infarction as non-diabetic patients with CHD [9]. These data provide a rationale for treating cardiovascular risk factors in diabetic patients as aggressively as non-diabetic subjects in the high-risk CHD category. For diabetic patients without pre-existing CHD, the current American Diabetic Association (ADA) goal for LDL-C is < 2.6 mmol/l (100 mg/dl) [3,10]. The recommendations of the ADA for the treatment of elevated LDL-C generally follow the guidelines of the NCEP [11], which state that diabetic subjects with clinical CHD and an LDL-C level of > 2.6 mmol/l (100 mg/dl) after behavioural and glucose interventions should be treated with pharmacological agents. Despite the recommendations recent data suggest that only a small proportion of type 2 diabetic patients achieve and sustain target LDL-C levels of < 3.4 mmol/l (130 mg/dl) to impact on cardiovascular morbidity [12–14].

The objectives of this study were to assess the efficacy and safety of 10–80 mg atorvastatin for the treatment of hyperlipidemia in type 2 diabetes patients with LDL-C levels ≥ 3.4 mmol/l (130 mg/dl). Atorvastatin is a synthetic HMG-CoA reductase inhibitor which has been shown to be highly effective at lowering LDL-C and triglyceride levels in non-diabetic patients. In hyperlipidemic subjects, doses of atorvastatin from 10–80 mg once-daily have been shown to reduce LDL-C levels by 41–61% [15] and triglycerides by 23–45% [16].

2. Materials and methods

2.1. Patients

All patients were previously diagnosed with type 2 diabetes according to the criteria of the ADA and had to have HbA1c < 10 for at least 4 weeks prior to screening for the trial. Patient characteristics at baseline are detailed in Table 1. The trial included men and post-menopausal or non-pregnant women aged between 18 and 80 years who had a Body Mass Index of ≤ 30. Plasma LDL-C levels in these patients were > 3.4 mmol/l (130 mg/dl) after the initial 6 weeks of isocaloric diet.

Patients were excluded if they had type 1 diabetes, uncontrolled hypertension, severe renal dysfunction, nephrotic syndrome or dysproteinemias, fasting plasma triglycerides > 10 mmol/l, aspartate aminotransferase (AST) or alanine aminotransferase (ALT) levels > 1.5 × the upper limit of normal (ULN), or if their creatine phosphokinase (CPK) levels were > 3 × ULN. Consumption of any lipid-altering drug within the previous 4 weeks (6 months for probucol) prevented entry into the study. None of the study subjects had tendinous xanthomata.

The protocol was approved by an Ethics Committee of every Institution and every patient provided witnessed, written, informed consent prior to entering the study.

2.2. Study design

This was a multicenter, open-label, 34-week dose- titration study (Fig. 1). Patients attended an initial
screening visit followed by a qualifying visit 4 weeks later in which compliance with diet was assessed and blood samples were taken. Within 2 weeks patients returned for a baseline visit during which further blood samples were tested and drug treatment was initiated. Changes in lipid profile after periods of treatment with atorvastatin were compared against the mean laboratory parameters obtained during the qualifying (week 2) and baseline (week 0) visits.

Throughout the trial, including the pre-treatment period of 6 weeks, patients were required to comply with an isocaloric, standard lipid-lowering diet defined by a registered dietician of 50% carbohydrates, 20% protein, 30% fat and 30 g/day fiber. Dietary advice was given at the initial visit and compliance with the diet assessed at every subsequent visit (at 4-week intervals) using a 3-day food record. Drug compliance and efficacy, as well as laboratory parameters were also measured at every visit.

2.3. Dose titration

The starting dose of 10 mg/day was doubled every 4 weeks until either the desired LDL-C level (≤ 2.6 mmol/l [100 mg/dl]) or a maximum dose of 80 mg atorvastatin once daily were achieved. Once patients had achieved their target LDL-C level, they maintained the same dose regimen for a further 16 weeks of treatment.

2.4. Efficacy parameters

At the end of the 16-week treatment period, efficacy parameters at the dose at which patients achieved the LDL-C target were compared with baseline values. In all cases, baseline values were averaged from measurements at the qualifying (Week 2) and baseline (Week 0) visits, whilst post-treatment values refer to the mean at Weeks 12 and 16 of treatment.

The primary efficacy parameters of the study were percentage changes in LDL-C and triglycerides from baseline. Secondary efficacy parameters included the percentage changes in total cholesterol, HDL-C, VLDL-C, and apolipoproteins A1 and B from baseline.

2.5. Safety evaluation

Before entering the study patients underwent a complete physical examination with clinical laboratory evaluation including blood count, measurement of thyroid-stimulating hormone (TSH) and CPK levels, urinalysis, liver function tests (ALT and AST), glycemic profile (fasting plasma glucose, HbA1c and fructosamine) and a pregnancy test. These tests were repeated at the end of the study. At each visit, liver function tests, glycemic profile and CPK levels were measured. Clinically important events were defined as: CPK > 5 × ULN at two consecutive measurements 1 week apart accompanied by muscle pain, tenderness or weakness; CPK > 10 × ULN at any time; ALT or AST > 3 × ULN at two consecutive measurements 1 week apart. Patients were excluded from the study if they developed severe hyperglycemia or any other significant deviation from safety tests. Other reasons for dismissal were lack of compliance to the drug or diet.

2.6. Laboratory analyses

The laboratory of the Departamento de Diabetes y Metabolismo de Lipidos of the Instituto Nacional de la Nutricion in Mexico performed all lipid and clinical laboratory measurements using standardized procedures. This laboratory is certified for standardization of tests by the External Comparative Evaluation of Laboratories Program of the College of American Pathologists. Blood samples were taken after an overnight fast (≥ 9 h). All laboratory analyses were performed with commercially available standardized methods. Glucose was measured using the glucose oxidase method and HbA1c using latex immunoagglutination inhibition (Bayer laboratories) [17]. Total serum cholesterol and triglycerides were measured using an enzymatic method (SERA-PAK®) (CV 3.3%). HDL-C levels were assessed using phosphotungstic acid and Mg$^{2+}$ (CV 2.5%). LDL-C concentration was estimated by the Friedewald formula [18]. Direct LDL-C was determined by ultracentrifugation (β quantification) at Week 0, on completion of 16 weeks of treatment and in every patient in whom triglyceride levels were > 4.5 mmol/l (400 mg/dl) [19]. Apolipoprotein B concentration was measured by an immunonephelometric method. Fructosamine concentration was measured using a reduction test with nitroblue tetrazolium (Bohringer–Mannheim).
2.7. Statistical analysis

Statistical analysis was performed with the SAS Statistical Package version 6.12 TS020. All differences between groups were evaluated using two-tailed paired $t$-tests.

### Table 2

<table>
<thead>
<tr>
<th>Atorvastatin dose (mg/day)</th>
<th>Baseline LDL-C level (mmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>4.3 ± 0.7</td>
</tr>
<tr>
<td>20</td>
<td>4.7 ± 0.7</td>
</tr>
<tr>
<td>40</td>
<td>5.4 ± 0.6</td>
</tr>
<tr>
<td>80</td>
<td>6.2 ± 1.7</td>
</tr>
</tbody>
</table>

3. Results

3.1. Patients

One hundred and ninety-four patients were screened for the study. The characteristics and baseline measurements of the patients who entered the study are shown in Table 1. A total of 102 patients satisfied the inclusion/exclusion criteria and entered the trial. Eighty-eight patients completed the study; 14 patients were not considered in the final analysis due to lack of compliance ($n = 10$), withdrawal due to adverse events ($n = 2$) or administration difficulties ($n = 2$).

3.2. Efficacy

All 88 patients who completed the study attained the target LDL-C level of $\leq 2.6$ mmol/l (100 mg/dl). Of these patients, 52 (59%) achieved their LDL-C goal with the 10 mg/day atorvastatin dose, 26 (29.5%) with the 20 mg dose, six (7%) with the 40 mg dose and four (4.5%) with the 80 mg dose. As expected the main determinant of the dosage needed to achieve the LDL-C goal was baseline LDL-C level (Table 2). When patients were stratified by their baseline LDL-C levels, 67 (76%) patients who finished the study had a baseline LDL-C of $\geq 5.2$ mmol/l (200 mg/dl). Of these patients, 47 (70.1%) achieved their LDL-C goal with the 10 mg/day atorvastatin dose, 17 (25.4%) with the 20 mg/day dose and only three (4.5%) required a 40 mg dose or greater. Of the 21 patients finishing the study whose baseline LDL-C was $\geq 5.2$ mmol/l (200 mg/dl), 14 (66.7%) required 20 mg/day or less to achieve the LDL-C goal. The highest dose (80 mg/day) was required in only three cases.

A 16-week treatment period of atorvastatin (10, 20, 40 or 80 mg) in 88 patients with type 2 diabetes resulted in a mean reduction from baseline in plasma LDL-C of 50% ($4.6 \pm 0.9$ mmol/l [177 ± 34 mg/dl] to $2.2 \pm 0.4$ mmol/l [87 ± 16 mg/dl], $P < 0.0001$) and a mean reduction in triglyceride levels of 18% ($2.7 \pm 1.8$ mmol/l [240 ± 164 mg/dl] to $2.1 \pm 1.1$ mmol/l [183 ± 95 mg/dl], $P < 0.0001$) (Fig. 2). During this period there was no significant change in Body Mass Index. The majority of patients achieved the target level of $\leq 2.6$ mmol/l (100 mg/dl) at the 10 mg dose of atorvastatin ($n = 52$, 59.1%) (Fig. 3). A total of 26 (29.5%) patients required titration to 20 mg/day; six (6.8%) required titration to 40 mg/day, and only four (4.5%) required titration to 80 mg/day.

The effect of atorvastatin on the lipid profile showed a dose-dependent trend although this was not tested statistically (Table 3). After 16 weeks of treatment at the effective dose, patients showed mean decreases in plasma LDL-C of 47.1, 53.0, 59.9 and 53.0% at daily
doses of 10, 20, 40 and 80 mg atorvastatin, respectively. At the same doses plasma triglyceride levels were reduced by 13.6, 19.4, 22.2 and 52.4%, respectively. The variable effects of the 80 mg dose may be explained in part by the low sample size (n = 4).

Mean values for the secondary efficacy parameters revealed that VLDL-C was significantly reduced from baseline by 33.1% from 1.7 ± 1.2 mol/l to 0.9 ± 0.6 mol/l (P < 0.0001) (Table 4). Apolipoprotein B levels were reduced from baseline by 37.4% from 1.44 ± 0.29 g/l to 0.88 ± 0.17 g/l (P < 0.0001). Patients showed a small but significant decrease in apolipoprotein A1 levels (4.6%, P < 0.0001). There was a trend toward increased plasma HDL-C (3.8%), but this did not reach significance in this patient group (P < 0.06). Importantly, the lack of effect on HbA1c indicates that the patients remained under adequate diabetic control.

### 3.3. Safety

The safety analysis included all patients entering the study (n = 102). Adverse events that may have been related to drug treatment were mild-to-moderate and reported by 8 (7.8%) patients. Two patients withdrew from the study because of adverse events. Only one was possibly attributable to the study drug in a patient who experienced a mild generalized rash after 4 weeks of 10 mg/day atorvastatin. A brain tumor was diagnosed during the first week of treatment in other case. No correlation between the incidence of potentially drug-related adverse events and drug dosage was observed in this study. There were no incidents of myopathy or liver dysfunction. No persistent elevations in ALT, AST or CPK, defined as clinically important, were reported during the course of the study.
4. Discussion

Lipid abnormalities are common in patients with type 2 diabetes. However, dyslipidemias are inadequately controlled in a substantial proportion of type 2 diabetic patients, suggesting that few achieve and sustain lipid goals recommended by international guidelines. This is a serious concern as it is well established that type 2 diabetics are at a significantly greater risk of CHD or arteriosclerotic vascular conditions than patients without diabetes. The strong association of increased concentrations of LDL-C with coronary artery disease in diabetic patients [12] suggests that physicians should adopt a more aggressive lipid-lowering strategy in this patient population. This approach is supported by a recent Finnish population-based study which has demonstrated that type 2 diabetic patients without a history of myocardial infarction have a similar prognosis to non-diabetic patients with a prior myocardial infarction [9].

Statins reduce hepatic cholesterol synthesis by inhibition of HMG-CoA reductase, a major enzyme involved in synthesizing cholesterol in the liver. Consequent depletion of hepatic cholesterol results in up-regulation of LDL receptors and increased hepatic removal of LDL-C. The long half-life of atorvastatin compared with other statins results in impressive cholesterol-lowering efficacy. Atorvastatin also significantly reduces VLDL-C, increased levels of which are one of the characteristics of diabetic dyslipidemia.

In non-diabetic populations, previous studies have demonstrated that atorvastatin is a highly effective and safe drug for the treatment of dyslipidemia. In the CURVES study treatment with atorvastatin 10–40 mg resulted in significantly greater reductions in plasma LDL-C than simvastatin, pravastatin, lovastatin, and fluvastatin [20]. In addition, a study comparing the cost-effectiveness of statin therapies showed that significantly greater proportions of patients achieve their NCEP LDL-C targets with atorvastatin [21]. In the study of patients with CHD, or risk factors for CHD, 90% of atorvastatin-treated patients reached their NCEP goal compared with 79% for simvastatin and lovastatin, and 55% for fluvastatin-treated patients (P < 0.05) at median doses of 10, 40, 80 and 40 mg, respectively [21].

In the current study treatment with atorvastatin resulted in a mean reduction in LDL-C of 50% across all of the doses (P < 0.0001). In the majority of patients (59%), target LDL-C levels of ≤2.6 mmol/l (100 mg/dl) were achieved at the starting dose of 10 mg atorvastatin.

These data support the findings of previous studies [15,16]. A retrospective, pooled analysis of 21 studies has demonstrated that atorvastatin 10 mg/day reduced LDL-C by 36% in type 2 diabetic patients (n = 156) [22]. Triglyceride and apolipoprotein B levels were also reduced by 21 and 29%, respectively. The authors of this pooled analysis concluded that atorvastatin can be used effectively in the diabetic patient population [22]. An open-label study has directly compared the efficacy parameters of atorvastatin 10 mg versus simvastatin 10 mg over a 4-week period in 25 type 2 diabetic patients [6]. Atorvastatin led to significantly greater reductions in total cholesterol (−30 vs. −24%) and LDL-C (−39 vs. −30%) compared with simvastatin [6].

Analysis of secondary efficacy parameters has demonstrated that atorvastatin caused a 33% reduction in plasma VLDL-C. Atorvastatin also markedly reduced triglyceride levels by 18%. In previous studies atorvastatin has been shown to have significantly greater triglyceride-lowering properties than other statins at starting doses (23–25). In the three, 1-year, double-blind clinical studies comparing the effects of atorvastatin (10 mg/day) versus either lovastatin (20 mg/day), pravastatin (20 mg/day) or simvastatin (10 mg/day) in patients with primary hypercholesterolemia, atorvastatin resulted in a significantly greater reduction in triglycerides: −16 versus −8% [23], −17 versus −9% [24] and −23% versus −15% [25], respectively.

As hypertriglyceridemia is one of the most common lipid imbalances in type 2 diabetic patients, atorvastatin may therefore offer greater benefits than other statins in this patient group.

The decrease in triglycerides may be explained by a reduction in both VLDL- and LDL-triglycerides. The data suggest that atorvastatin not only reduces the number of LDL particles but also decreases VLDL secretion. Other mechanisms to explain the triglyceride reduction are unlikely as the statins do not affect the activity of the lipolytic enzymes or the remnant receptor activity [26]. This interpretation is in agreement with a recent report in which atorvastatin decreased both plasma cholesterol in familial hypercholesterolemia (FH) subjects with no functional LDL receptors and the cholesterol rebound observed after LDL-apheresis [27,28]. Further support for this statement is provided by the magnitude of cholesterol lowering in patients with homozygous and heterozygous FH. Atorvastatin 80 mg/day results in an LDL-C reduction of approx. 25% in homozygous FH and approx. 55% in heterozygous FH [29]. If the inhibition of VLDL secretion were the most important aspect of atorvastatin’s mechanism of action, the magnitude of the lipid-lowering effect between the two forms of FH would not be so different. Assuming that the rate of the atorvastatin-induced inhibition of VLDL secretion is the same in both conditions, the percentage of the LDL-C reduction attributable to this mechanism is 44% at most. There is also no correlation between a reduction in urinary mevalonic acid levels, as an index of in vivo cholesterol synthesis, and statin-induced reduction in apolipoprotein B levels [30].
The safety analysis of this study demonstrates that atorvastatin has a good tolerability profile [22,6]. Adverse events reported that were potentially related to drug use were all mild-to-moderate in intensity with headache and inferior extremity pain being the most common. The incidence of adverse events was unrelated to dosage. Only one patient withdrew from the study due to a possible atorvastatin-related adverse event. No patients in this study experienced statistically relevant elevations of CPK. Furthermore, atorvastatin did not effect glycemic control in these patients. Although a small but statistically significant increase in fasting glucose was observed, the increase was not dose-related and there was no increase in HbA1c.

Although the most frequent lipoprotein abnormalities in this type of diabetes are an increase in triglyceride-rich lipoproteins and a decrease in high-density lipoproteins, hypercholesterolemia is as powerful a predictor of CHD risk in diabetic patients as in non-diabetic subjects. In spite of this knowledge, there is to date no solid evidence to indicate whether correction of dyslipoproteinemia in order to reduce CHD risk in patients with type 2 diabetes is more, equally, or less beneficial than it is in non-diabetic subjects [31]. The only currently available data come from post-hoc subgroup analyses of the Helsinki Heart Study [32] and the Scandinavian Simvastatin Survival Study [7].

Long-term morbidity and mortality studies with atorvastatin have not yet been completed. However, in order to investigate the benefits of aggressive lipid-lowering in the prevention of CHD in patients with type 2 diabetes, several clinical endpoint trials are underway. The Atorvastatin Study for the Prevention of Coronary Heart Disease Endpoints in patients with non-insulin-dependent diabetes mellitus (ASPEN) will compare treatment with once-daily atorvastatin 10 mg versus placebo over 4 years. Centers in the USA, Canada, Europe, South Africa and Australia will study approximately 2250 diabetics. In the UK, the Collaborative AtoRvastatin Diabetes Study (CARDS) will follow 2100 diabetic patients without a history of myocardial infarction who are being treated with either once-daily atorvastatin 10 mg or placebo over a 5-year period. Lipid entry criteria for both ASPEN and CARDS are LDL-C ≤ 4.1 mmol/l (160 mg/dl) and triglycerides ≤ 6.8 mmol/l (600 mg/dl).

In conclusion, atorvastatin is a well tolerated and very efficacious member of the statin class of drugs. In this trial significant reductions in total cholesterol (34%), LDL-C (47%) and apolipoprotein B (34%) were achieved with the lowest dose of atorvastatin (10 mg/day). The 10 mg dose lowered LDL-C to ≤ 2.6 mmol/l (100 mg/dl) in 59% of patients. Even greater reductions are achievable with larger doses. These results clearly show that atorvastatin will enable the majority of type 2 diabetes hyperlipidemic patients to achieve primary and secondary prevention goals for lipid reduction without the need for complex regimens of several drugs. In type 2 diabetes patients with a baseline LDL-C of < 5.2 mmol/l (200 mg/dl), atorvastatin 10 mg/day will allow the majority of patients to achieve the goals of an aggressive lipid-lowering therapy. The current study demonstrates that the beneficial effects of atorvastatin can be extended to include type 2 diabetes patients. All patients who completed the 16-week trial attained the target LDL-C level of ≤ 2.6 mmol/l (100 mg/dl). The majority of patients (59%) achieved this level at the 10 mg starting dose of atorvastatin. At this dose atorvastatin was also effective at reducing triglycerides by 13.6% and VLDL-C by 29.3%. The lipid-lowering effects achieved at the 10 mg dose confirm that atorvastatin is a very useful agent for the treatment of lipid abnormalities in patients with type 2 diabetes.

References


