

The Atorvastatin Goal Achievement Across Risk Levels: (ATGOAL) Study in Thailand

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Objective: To evaluate the efficacy and safety of atorvastatin at the starting doses of 10, 20, 40 mg and evaluate the effectiveness of 1 step titrate up regimen.

Material and Method: Two hundred and forty two subjects with dyslipidemia were enrolled and assigned the appropriate dose in relation to their individual cardiovascular risk status and baseline LDL-C levels. If the NCEP targets were not achieved, the doses were titrated up at week 4 and the primary efficacy was evaluated at week 8.

Results: A majority of subjects (88.8%) achieved their LDL-C goals at week 8. Almost all of the subject's LDL-C levels reached their goals by week 2 and 4 (81.6% and 87.1%, respectively). Only 10.7% (n=25) required the sole titration. Each dose provided significant decreases in LDL-C (average -46.4%). Only 36 subjects experienced treatment related adverse events, the majority of these were in the high-risk group (n=22) with only one subject registering a serious adverse event.

Conclusion: Atorvastatin is effective and safe for Thai patients with dyslipidemia. The appropriate starting dose has contributed in the achievement of cholesterol reduction.

Keywords: Atorvastatin, Dyslipidemia, Treatment

J Med Assoc Thai 2007; 90 (1): 72-81

Full text. e-Journal: <http://www.medassocthai.org/journal>

Cardiovascular diseases (CVD) are the leading cause of death in most countries in the world-with emphasis on coronary heart disease (CHD), peripheral arterial disease (PAD), and stroke (cerebrovascular accident)^(1,2). According to the World Health Organization (WHO) estimates, 17 million people die of CVD each year. In 1998, there were 7.3 million deaths from heart attack and 5.1 million from stroke. The WHO predicts that in 2020, there will be 11.1 million deaths from CHD⁽³⁾. In Thailand, CHD was one of the leading causes of death in 2001 (the death rate was 30.3 per 100,000 population and 182.2 per 100,000 in the elderly age group)⁽⁴⁾. The well-established risk factors of CVD include hypercholesterolemia (especially high low

density lipoprotein-cholesterol [LDL-C], low high density lipoprotein-cholesterol [HDL-C]), hypertension, smoking, diabetes mellitus, and physical inactivity⁽⁵⁻⁷⁾. Results from many clinical trials have shown that reducing plasma LDL-C levels significantly reduces the risk for CHD and leads to both primary⁽⁸⁻¹⁰⁾ and secondary⁽¹¹⁻¹⁴⁾ prevention of cardiovascular disease.

The National Cholesterol Education Program Adult Treatment Panel (NCEP ATP) III⁽¹⁵⁾ and the Third Joint Task Force of European and Other Societies guidelines⁽¹⁶⁾ recommend LDL-cholesterol target levels of lower than 100 mg/dL (2.6 mmol/L) in high-CHD risk patients, and recently the Coordinating Committee of NCEP has recommended that clinicians consider an LDL-cholesterol goal of < 70 mg/dL (1.8 mmol/L) as a therapeutic option for very high-risk CHD patients. With clinical evidence, the NCEP ATP III panel expanded the

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scope and intensity of LDL lowering therapy for higher risk individuals beyond that of previous NCEP ATP versions.

Although pharmacological treatments are available that effectively lower LDL-cholesterol, many patients fail to achieve and maintain target LDL-cholesterol levels. In 1997, a therapeutic survey called the Lipid Treatment Assessing Program (L-TAP) was conducted in the United States⁽¹⁷⁾ which reported overall achievement rates at 38% of patients. Similarly, the first L-TAP study in Thailand⁽¹⁸⁾ that took place in the same year reported very low rates of achievement of cholesterol therapy (overall success rate of 40.5%) in the patients with dyslipidemia and reported that only 41.2% of patients were treated with statins. Five years after the first evaluations were made, the L-TAPII survey was repeated to reevaluate cholesterol treatment in Thailand⁽¹⁹⁾. A total of 34.6% of patients with CHD or CHD equivalent risk, 56.4% of high risk and 76.8% of low risk subjects achieved their LDL-C targets as defined by NCEP ATP III - an overall of 46.5% achievement rate. From the study population, 64% of the patients used either statins alone or a combination with statins. These studies demonstrate that although statins are effective in lowering LDL-C, there is a lower than optimal dosage being prescribed in treating dyslipidemia.

Atorvastatin has been shown to reduce LDL-cholesterol from 25% to 61% over the 2.5 mg to 80 mg dosing range^(20,21). The New Atorvastatin Starting Doses (NASDAC)⁽²²⁾ study also tied higher LDL-C reductions across starting doses of 10, 20, 40 and 80 mg (-35.7%, -42.2%, -48.6% and -52.2% respectively). Subgroup analysis shows that a significantly more percentage of patients that achieve LDL-C goals with and without CHD risk factors increase when comparing 10 mg to 80 mg doses.

The safety of atorvastatin has also been evaluated and confirmed from pooled data from 44 clinical trials comprising of 9,416 patients across the dose ranges of 10 to 80 mg⁽²³⁾. The Treating to New Targets trial (TNT)⁽²⁴⁾ also revealed similar results analyzing a population of 10,001 subjects. The overall incidence of adverse events (AE) of atorvastatin-treated patients was low and comparable with that found in placebo and other statins. Likewise, Jones et al reported that doses of atorvastatin ranging from 10 mg to 80 mg reported no dose response relationship with regards to the overall incidence of AEs. The most frequently occurring adverse event was myalgia and all AEs were mild or moderate in severity⁽²²⁾.

The present study was designed to assess whether atorvastatin treatment in Thai dyslipidemic patients results in a quick achievement of LDL-C target with either no titration, or just 1 titration step, provided the starting dose was appropriate for the level of LDL-C reduction required. As such, subjects were assigned to an atorvastatin starting dose according to their LDL-C level and their individual CHD risk categorization (as defined by NCEP ATP III) upon entry. A subject's target LDL-C level was dependent upon their baseline LDL-C level and their CHD risk assessment.

Material and Method

Study design

The present study was an 8-week prospective, multicenter, open-label study of atorvastatin for treatment of dyslipidemia in Thai subjects. The present study was carried out over 8 months at nine study sites in Thailand. For subjects, a target LDL-C, according to their individual cardiovascular risk categorization (defined by the NCEP ATP III) and their LDL-C at baseline was determined prior to the study start. An atorvastatin starting dose (10, 20 or 40 mg/day) was thus determined (Table 1).

Serum lipid levels were evaluated at weeks 2, 4 and 8. Subjects who achieved their LDL-C target by the week 4 visit continued on their starting dose for the remaining 4 weeks; subjects who did not achieve their LDL-C target by the week 4 visit were titrated up 1 dose step for the remaining 4 weeks (i.e., 10 mg to 20 mg; 20 mg to 40 mg and 40 mg to 80 mg).

Patient population

Study patients were outpatient Thai men and women aged between 18-80 years, diagnosed with dyslipidemia, and followed the Therapeutic Lifestyle Changes (TLC) diet for at least 1 month prior to screening. Those with prior antilipidemic medication were required to have a 6 week washout period prior to screening. They should be eligible for LDL lowering drug therapy at baseline as determined by the following NCEP ATP III LDL-C cut off points:

LDL-C \geq 190 mg/dL for subjects with 0 or 1 CHD risk factor

LDL-C \geq 160 mg/dL for subjects with 2 or more CHD risk factors and 10-year risk < 10%

LDL-C \geq 130 mg/dL for subjects with 2 or more CHD risk factors and 10-year risk 10-20%

LDL-C \geq 100 mg/dL for subjects with documented CHD or CHD risk equivalents (10-year risk > 20%)

Table 1. Initial dose assignment of atorvastatin (mg) according to cardiovascular risk category and baseline LDL-C

	Cardiovascular Risk Category (no. of risk factors, 10-year risk)			
	Category 1 (0-1, N/A)	Category 2 (2+, <10%)	Category 3 (2+, 10-20%)	Category 4 (CHD, >20%)
LDL-C at Baseline*				
100-129 mg/dL	-	-	-	10
130-149 mg/dL	-	-	10	10
150-159 mg/dL	-	-	10	20
160-179 mg/dL	-	10	10	40
180-189 mg/dL	-	10	20	40
190-220 mg/dL	10	20	20	40
LDL-C Target (mg/dL)	<160	<130	<130	<100

N/A, not applicable

*At baseline and/or screening (dependent on whether a subject required a 6-week washout or not)

LDL-C, low density lipoprotein-cholesterol

Exclusion criteria included those with a history of intolerance or hypersensitivity to statins, levels of LDL-C > 220 mg/dL and triglyceride level > 600 mg/dL, a progressive fatal disease with a life expectancy of under 2 years, impaired hepatic function defined by aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 2 times of the upper limit of normal (ULN) at baseline. Additionally, they did not have uncontrollable hypertension, drug/alcohol abuse, gastrointestinal disease limiting drug absorption or partial ileal bypass, planned elective surgery during the study and any severe disease or major problem or surgical procedure within 3 months prior to screening. Pregnant or lactating women were also excluded as were individuals with secondary causes of hyperlipoproteinemia, defined as uncontrolled primary hypothyroidism (thyroid-stimulation hormone ≥ 1.5 x ULN), blood urea nitrogen ≥ 30 mg/dL, creatinine ≥ 2.0 mg/dL or creatine kinase (CK) ≥ 3 x ULN at baseline. Those that participated in another study involving investigational or marketed products within 30 days prior to entry into the present study, had a mental condition that renders the subject unable to understand the nature, scope, and possible consequences of the present study, and/or demonstrated evidence of an uncooperative attitude were all excluded.

The study protocol was approved by an institutional review board of each study site and conducted in compliance with the ethical principles of the most recent version of the International Conference of Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, all local regulatory requirements and the

Declaration of Helsinki. All patients gave written informed consent.

Evaluation of efficacy and safety

The primary efficacy variable was the percentage of subjects who achieved LDL-C target at week 8. Secondary variables included the percentage of subjects who achieved LDL-C target at week 2, 4 and 8 with 1 step titration; the change and percent change from baseline at weeks 2, 4, 8 for LDL-C, high density lipoprotein-cholesterol (HDL-C), LDL/HDL ratio, total cholesterol (TC) and triglycerides.

Evaluations of safety were based on physical examinations, vital signs and body weight, and adverse events along with clinical laboratory tests (i.e. a complete blood count; fasting blood sugar, liver function test, blood urea nitrogen, creatinine, potassium, creatine phosphokinase, and urinalysis). Treatment-emergent AEs were events that emerged during the treatment phase or that increased in severity from baseline. Serious adverse events were events that resulted in death, were life-threatening, required or prolonged hospitalization, resulted in persistent or significant disability/incapacity, and congenital abnormalities/birth defects.

Statistical method

The sample size was determined to provide an accurate estimate of the treatment target response rate (the percentage of subjects achieving their designated LDL-C target at week 8. It was estimated that a sample size of 240 would provide a 95% CI of 66-79%, which is within $\pm 10\%$ of the observed response rate,

assuming a 10% dropout and an observed response rate of 72.5%. For subgroup analysis, subjects were classified at baseline into three risk groups (i.e. low, medium, high risk group) according to their baseline risk level with respect to CHD as defined by NCEP ATP III.

Descriptive statistics for efficacy and safety data were used. All efficacy variables were analyzed for the intent-to-treat (ITT) population, and repeated/confirmed for the evaluable (EVAL) population. The ITT population was defined as subjects who took at least one dose of the study drug and had a post baseline lipid assessment. The EVAL population consisted of a subset of subjects who satisfied the ITT criteria, who met the inclusion/exclusion criteria and who adhered strictly to the conditions of evaluability in being assigning correct doses at baseline and week 4, 80% > 120% medication compliant at both Weeks 4 and 8 and had no major protocol violations.

Results

Study population

Three hundred and twenty two individuals were screened and 242 (100%) were treated with the study medication. The ITT and EVAL populations were 240 (99.2%) and 220 patients (90.9%) respectively. Eleven (4.5%) subjects were discontinued from the present study. The majority of discontinuations (7 subjects) were not related to the study drug with only four (1.6%) cases related to the study drug.

Demographic and Baseline Characteristics

The mean duration of diagnosis of dyslipidemia was 3.6 years (range 0.0-26.4 years). After categorization according to NCEP ATP III guidelines, a majority of the patients were categorized as high risk (66.5%) (Fig. 1). Most of the present study population was female except in the medium risk. The low risk group was the youngest in age and had the lowest weight as shown in Table 2.

A majority of each patient in each risk group were assigned 10 mg of atorvastatin as shown in Table 3. The initial dose of 40 mg was assigned only to 65 subjects in the high risk group. The overall majority of subjects (54.1%) were assigned to 10 mg/day atorvastatin at baseline (19.0%, 20 mg/day and 26.9%, 40mg/day).

At week 4, 25 subjects (10.7%) were titrated up 1 step. As a whole, the number of subjects assigned to 10, 20, 40 and 80 mg/day atorvastatin at week 4 were 114 (48.9%), 55 (23.6%), 52 (22.3%) and 12 subjects

(5.2%) respectively. Of the subjects that were titrated at week 4 (i.e., had not reached their LDL-C target), 52% went on to reach their target by week 8.

Efficacy evaluation

Primary efficacy

In the total study population, 88.8% and 91.4% of subjects achieved their LDL-C target at week 8 for the ITT and EVAL groups respectively (Table 4).

Secondary efficacy

The percentage of LDL-C responders at week 2 and 4

Both the ITT and EVAL groups showed high values for the percentage of subjects who achieved their target LDL-C levels as soon as week 2 and 4. The overall ITT values are at 81.6% and 87.1% for week 2 and 4 respectively while the EVAL group recorded 83.2% and 90.0% success respectively (Table 4).

The percentage of LDL-C responders at week 8 with 1 step titration

The 25 subjects whom did not reach their LDL-C target were titrated up one step. The majority of the subjects were in the high risk group (18 subjects (72.0%)) while the medium risk group had two subjects (8.0%) and the low risk having five (20.0%). Of the subjects titrated, 52% reached their target by Week 8, 2 (40%) subjects for the low risk; 1 subject (50%) for the medium risk; and 10 patients (56%) for the high risk.

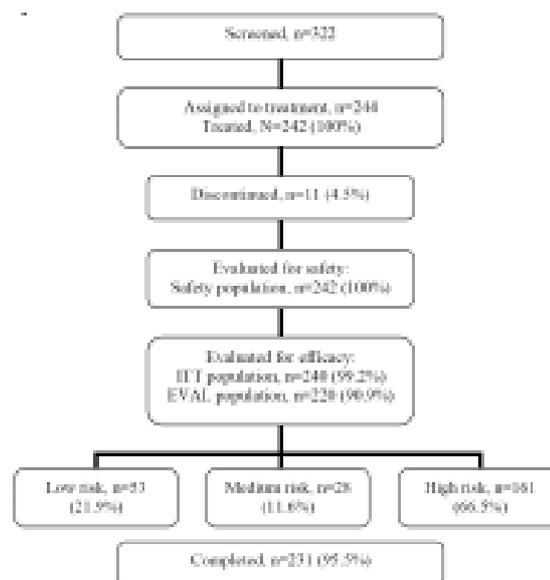


Fig. 1 Overview of subject disposition

Table 2. Demographic and baseline characteristics

	Total	Low risk (n = 53)	Medium risk (n = 28)	High risk (n = 161)
Mean Age, yrs (SD)	56.1 (11.0)	52.1 (11.2)	57.7 (6.3)	57.1 (11.3)
Sex [n (%)]				
Male	80 (33.1)	9 (17.0)	20 (71.4)	51 (31.7)
Female	162 (66.9)	44 (83.0)	8 (28.6)	110 (68.3)
Weight (SD) (kg)	65.4 (12.8)	62.7 (12.3)	69.1 (13.1)	65.6 (12.8)
Height (SD) (cm)	158.4 (8.4)	158.3 (7.9)	162.4 (9.2)	157.8 (8.2)

Table 3. Treatment assignment of atorvastatin at baseline - safety analysis population

Atorvastatin	Total (n = 242) n (%)	Low risk (n = 53) n (%)	Medium risk (n = 28) n (%)	High risk (n = 161) n (%)
10 mg	131 (54.1)	41 (77.4)	17 (60.7)	73 (45.3)
20 mg	46 (19.0)	12 (22.6)	11 (39.3)	23 (14.3)
40 mg	65 (26.9)	0	0	65 (40.4)

Table 4. Percentage of subjects that achieved LDL-C target by risk group at week 2, 4 and 8 by ITT and EVAL groups

	Low risk	Medium risk	High risk	Total
ITT Population	n = 52	n = 28	n = 160	n = 240
Week 2	80.4	82.1	81.9	81.6
Week 4	90.4	89.3	85.6	87.1
Week 8	90.4	92.9	87.5	88.8
EVAL Population	n = 45	n = 26	n = 149	n = 220
Week 2	82.2	84.6	83.2	83.2
Week 4	93.3	92.3	88.6	90.0
Week 8	93.3	96.2	89.9	91.4

Change and percent change from baseline in lipid parameters (LDL-C, HDL-C, LDL/HDL ratio, TC and triglycerides)

Atorvastatin reduced LDL-C, total cholesterol (TC) and triglycerides (TG) levels in all risk groups by an average of 46.4%, 34.6% and 22.5% respectively among the ITT population. An increase in HDL-C from baseline to week 8 was also observed in all treatment groups by an average of 3.3% (Table 5, Fig. 2). The LDL/HDL ratio equated to a 47.1% mean decrease and the results were similar across risk groups: low, 44.6%; medium, 46.7%; high, 47.9%.

Safety

Overall, 36 (14.9%) subjects experienced 45

treatment related AEs: low risk 10 (18.9%) subjects, medium risk 4 (14.3%) subjects, and high risk 22 (13.7%) subjects. Only seven treatment related AEs were recorded as severe i.e. asthenia, chest pain, anorexia, nausea, vomiting, weight loss and myalgia-all of which were experienced by one subject (0.4%) - it was concluded to have been non-treatment related. The commonly reported treatment related AEs are summarized in Table 6.

Eleven subjects discontinued from the present study with only four cases deemed to be related to the study drug. This could be broken down to two subjects in each of the low (3.8%) and high (1.2%) risk groups. Adverse events that occurred in the first three patients included hepatitis, headache, myalgia and CPK rising.

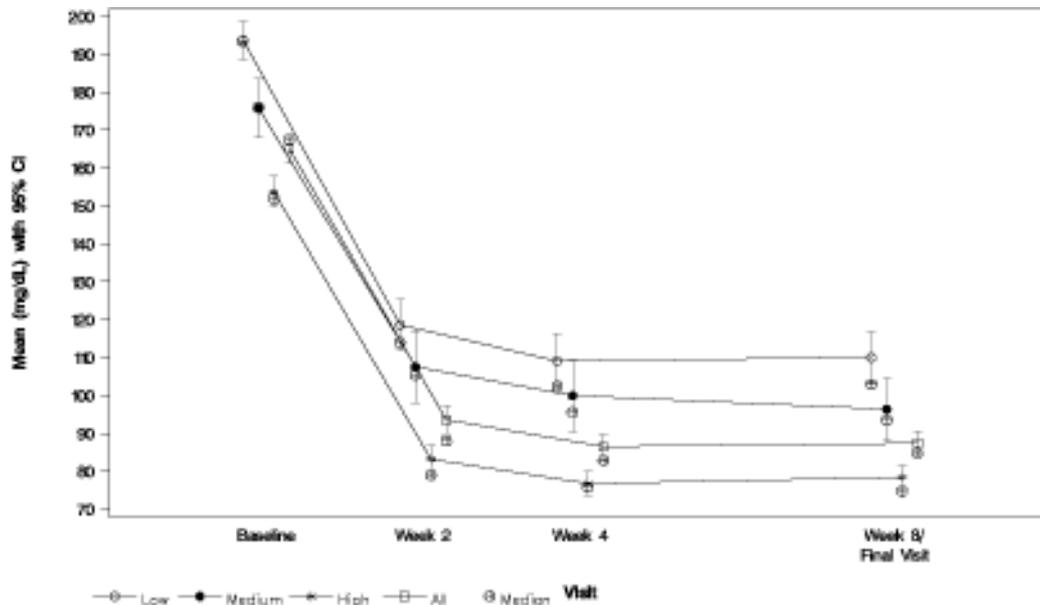


Fig. 2 LDL-C mean value by risk group over time (ITT Group) at baseline, week 2, 4 and 8

Table 5. Percent change from baseline in lipid parameters by risk group in the ITT group

	Total, n = 240 mean (95% CI)	Low risk, n = 52 mean (95% CI)	Medium risk, n = 28 mean (95% CI)	High risk, n = 160 mean (95% CI)
LDL-C	-46.4 (-48.3,-44.6)	-43.0 (-46.4, -39.5)	-44.6 (-49.7, -39.4)	-47.9 (-50.2, -45.6)
Triglycerides	-22.5 (-26.2, -18.8)	-17.1 (-25.2, -9.0)	-27.4 (-38.4, -16.4)	-23.4 (-28.0, -18.8)
TC	-34.6 (36.1, -33.2)	-32.9 (-35.3, -30.5)	-35.0 (-38.8, -31.2)	-35.1 (-37.0, -33.2)
HDL-C	3.3 (1.0, 5.7)	4.9 (0.6, 9.2)	6.2 (-3.1, 15.4)	2.3 (-0.6, 5.3)

Table 6. Treatment related AEs, experienced by more than one subject - safety population

Treatment related AE	n (%)
Myalgia	7 (2.9)
Anorexia	3 (1.2)
Hepatitis	3 (1.2)
Nausea	3 (1.2)
Constipation	2 (0.8)
Dizziness	2 (0.8)
Dyspepsia	2 (0.8)
Headache	2 (0.8)

acute bronchitis); however, both SAEs were not related to the study drug. One of the subjects discontinued prematurely from the present study while the other completed the study. Both subjects recovered from their SAE and both were taking 10 mg/day atorvastatin.

Eleven subjects (4.6%) had elevated creatine phosphokinase (CPK); greater than 2 times but less than 10 times that of ULN, without regard to baseline abnormality. CPK values for five of these subjects returned to < 2 times of ULN by the final visit. No subjects experienced extreme CPK elevation (> 10 times of ULN).

The other patient had fatigue, chest pains, anorexia, nausea, vomiting, weight loss, and myalgia.

Two subjects experienced a serious adverse event (SAE) (acute cholangitis/bile duct stone and

Discussion

The primary objective of this study was to determine the percentage of subjects achieving LDL-C target at week 8. In the total study population, a large

proportion of subjects (88.8%) achieved their target LDL-C by week 8; however, it is worth noting that 81.6% of subjects had achieved their LDL-C target by week 2, and that this response was sustained through to week 4 (87.1%) and continued until the end of the study (week 8). This result is comparable to another study in Asian subjects where 93% of subjects reached their target NCEP LDL-C⁽²⁵⁾ - the slightly higher value may be explained by the fact that it was a 16 week study, while the current study was carried out over 8 weeks.

As described, the total study population was divided into 3 categories (low, medium and high risk) dependent on starting LDL-C and CHD risk. The response (in terms of reaching LDL-C target) at week 2 was comparable across risk groups. At week 8, the response was slightly lower in the high risk group (87.5%) compared with the low (90.4%) and medium (92.9%) risk groups.

The majority (54.1%) of subjects were assigned 10 mg/day atorvastatin at baseline (19.0%, 20 mg/day and 26.9%, 40mg/day). In the total sample only 25 (10%) subjects who did not reach their LDL-C target were titrated up to the next dose level were titrated at week 4. The majority of these (n = 18) were in the high risk group, and only 12 subjects were assigned to 80 mg/day atorvastatin. Of the subjects that were titrated at week 4, 52% went on to reach their target by week 8.

The overall reduction for LDL-C was 46.4% for the total population. This result is comparable to published data from other studies in Asian populations where a 42% reduction has been observed after 8 weeks of treatment with 10 mg/day atorvastatin^(25,26). Across risk groups, greatest reduction in LDL-C was observed in the high risk group (low, 43.0%; medium, 44.6%; high, 47.9%). This is perhaps not surprising as subjects in the high risk group were treated more aggressively; 40.4% (n = 65) of the high risk group were assigned to 40 mg/day atorvastatin at baseline, with no subjects assigned 40 mg/day in either the low or medium risk groups.

In line with the reduction in LDL-C, TC was also reduced in subjects participating in the present study. Overall TC reduction was 34.6% for the total population. Across risk groups, the reduction in TC was slightly higher in the medium and high risk groups compared with the low risk (low, 32.9%; medium, 35.0%; high, 35.1%). Other studies in Asian populations have reported similar findings⁽²⁵⁻²⁷⁾. Wang et al, observed a 31% reduction in TC in Japanese subjects after 8 weeks of treatment with 10 mg/day atorvastatin⁽²⁶⁾.

Triglycerides were also reduced overtime during the present study. The overall reduction in triglycerides was 22.5% at week 8; this varied somewhat across risk group (low, 17.1%; medium, 27.4%; high, 23.4%). Again, these results are comparable to the findings of Wu et al, and Wang et al, who reported a 22% and 23% reduction in triglycerides, respectively; both studies used 10 mg/day atorvastatin^(25,26).

In the total population, HDL-C was only slightly increased over the 8 week duration of the present study (3.3% at Week 8); this result varied a lot across risk groups, with the lowest increase observed in the high risk group (4.9% low, 6.2% medium, 2.3% high). This result is similar to the findings of Wu et al, who reported a 4.6% increase in HDL-C after 8 weeks of treatment with 10 mg/day atorvastatin⁽²⁶⁾. However, the increase in HDL-C observed in the present study was low compared to 11% and 15%, which has been observed in Japanese subjects treated with 10 mg/day atorvastatin for 8 weeks^(26,27).

All doses of atorvastatin were well tolerated. In addition, the overall incidence and severity of AEs was generally low during the present study. Only 11 (4.5%) subjects prematurely discontinued from the present study; five discontinued as a result of AEs, four of them were treatment related and two of them were myalgia. As a whole, the number of myalgia reported in the present study (2.9%) was lower than other studies analyzing atorvastatin doses ranging from 10 mg and 80 mg^(22,24). There were no premature discontinuations from the present study due to abnormal laboratory test results. The incidence of abnormal laboratory test results was, for the most part, unremarkable. Importantly, no subject experienced extreme elevation of CPK (>10 x ULN), and there were no cases of rhabdomyolysis or myopathy reported during the present study.

In conclusion, Atorvastatin at the doses of 10, 20, 40, and 80 mg was found to be a highly effective, safe, and well tolerated statin treatment for dyslipidemia in this Thai sample population. The appropriate starting dose was a contributing factor in the achievement of cholesterol reduction.

Acknowledgements

This study was supported by a grant from Pfizer (Thailand) Limited. The authors wish to thank the following persons who participated in this study: Ms. Pattraporn Konthong (Rajavithi Hospital), Dr. Meta Phoojaroenchanachai, Dr. Apiradee Sriwijitkamol (Siriraj Hospital), Dr. Chesda Udommongkul, Dr. Pasiri

Sithinamsuwan (Pramongkutklao Hospital), Dr. Sompongse Suwanwalaikorn, Prof. Kammant Phanthumchinda, Dr. Aurauma Chutinet, Dr. Yuttachai Likitjaroen, (Chulalongkorn Memorial Hospital), Dr. Nakarin Sansanayudh (Pramongkutklao Hospital), Asst. Prof. Ampica Mangklabruks, Ms. Laddawan Limpijarnkit, Ms. Warangkana Mekara (Chiang Mai University).

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**การศึกษาประสิทธิผลของยาอะทอวาสแตตินในการบรรลุเป้าหมายของการลดระดับไขมันในเลือด
ในผู้ป่วยโรคหัวใจและหลอดเลือดและผู้ที่มีปัจจัยเสี่ยง**

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วัตถุประสงค์: เพื่อศึกษาประสิทธิผลและความปลอดภัยของยาอะทอวาสแตตินขนาดเริ่มต้น 10 มิลลิกรัม 20 มิลลิกรัม
หรือ 40 มิลลิกรัม โดยปรับขนาดยาหนึ่งครั้ง

วัสดุและวิธีการ: อาสาสมัครที่มีระดับไขมันผิดปกติในเลือดจำนวน 242 รายได้รับยาในขนาดที่เหมาะสมโดยขึ้นกับ
ภาวะของปัจจัยเสี่ยงโรคหลอดเลือดและหัวใจ และระดับ แอล ดี แอล โคเลสเตอรอล (LDL-C) ของผู้ป่วย ณ วันคัดเลือก
ถ้าระดับ แอล ดี แอล โคเลสเตอรอล (LDL-C) ยังไม่อยู่ในระดับที่ตั้งเป้าหมายไว้ตามเกณฑ์ NCEP จะมีการปรับขนาดยา
ในสัปดาห์ที่ 4 และจะมีการประเมินประสิทธิผลหลักในสัปดาห์ที่ 8

ผลการศึกษา: ในสัปดาห์ที่ 8 อาสาสมัครส่วนใหญ่ (88.8%) สามารถบรรลุเป้าหมายในการลดระดับ แอล ดี แอล โค
เลสเตอรอล (LDL-C) และเกือบทั้งหมดบรรลุเป้าหมายในการลดระดับ แอล ดี แอล โคเลสเตอรอลในสัปดาห์ที่ 2 และ
4 (81.6% และ 87.1 % ตามลำดับ) มีเพียง 10.7% ที่จำเป็นต้องปรับขนาดยา และยังพบว่ายาแต่ละขนาดสามารถ
ลดระดับแอล ดี แอล โคเลสเตอรอลลงได้อย่างมีนัยสำคัญทางสถิติ มีอาสาสมัครเพียง 36 รายที่พบว่ามีอาการไม่พึง
ประสงค์ที่มีความสัมพันธ์กับยา โดยส่วนใหญ่พบในอาสาสมัครที่มีปัจจัยเสี่ยงสูง (22 ราย) และมีเพียง 1 รายเท่านั้น
ที่มีอาการไม่พึงประสงค์ร้ายแรง

สรุป: ยาอะทอวาสแตตินมีประสิทธิผลและความปลอดภัยในอาสาสมัครชาวไทยที่มีระดับไขมันผิดปกติในเลือด และ
พบว่าทำให้ยาในขนาดเริ่มต้นที่เหมาะสมมีผลต่อความสำเร็จในการลดระดับ แอล ดี แอล โคเลสเตอรอลตามเป้าหมาย
ที่กำหนดไว้
