

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: None

ACTIVE INGREDIENT: None

Study No: NIS-CAP-DUM-2008/1

Centralized Pan-Asian survey on the Under treatment of hypercholesterolemia

Developmental phase: LCM

Study Completion Date: 31 December 2008

Date of Report: 01 December 2009

OBJECTIVES:

Primary objective

- To establish the proportion of patients on lipid-lowering pharmacological treatment reaching the LDL-C goals according to the updated 2004 National Cholesterol Educational Program Adult Treatment Panel III (NCEP ATP III) guidelines by assessment of blood lipid profile (overall and by country).

Secondary objectives

- To establish the proportion of patients on lipid-lowering pharmacological treatment reaching the LDL-C goals according to the updated 2004 NCEP ATP III guidelines in the following sub-populations: primary or secondary prevention patients, and patients with metabolic syndrome, as according to NCEP ATP III definition.
- To identify the determinants for undertreatment of hypercholesterolemia according to the updated 2004 NCEP ATP III guidelines by assessment of patient and physician characteristics.

To investigate patient and physician characteristics associated with the allocation of treatment approaches.

METHODS:

This was a multi-centre survey of patients on lipid-lowering pharmacological treatment for at least 3 months, with no dose change for a minimum of 6 weeks, prior to enrollment. The study was conducted in the following eight Asian countries: Korea, Thailand, Taiwan, Indonesia, Philippines, Malaysia, Hong Kong and Vietnam. The study included a single visit.

Before assessment of any patient, the physicians filled the physician questionnaire on their experience and perception of hypercholesterolemia management. The physicians were to indicate

their general attitude on the diagnosis of hypercholesterolemia, the lipid-lowering guidelines and goals, and the various treatment options for hypercholesterolemia.

Before being assessed by the physician, patients from all the participating countries recorded on the patient questionnaire their awareness of hypercholesterolemia, current lipid-lowering treatment and their perception of it, and treatment compliance. The physician completed the Case Record Form (CRF) with patient's demographics, results of physical examination, cardiovascular medical history, current lipid-lowering therapy and reason for the current therapy. A fasting blood sample was taken for the analysis of lipid profile and glucose.

The physicians determined whether patients had achieved their treatment goals based on the laboratory results and took appropriate measures, if any, with respect to the future treatment of the patients.

RESULTS:

The analysis of the primary and secondary variables as well as baseline assessments and analysis of patient questionnaire data were based on the PPS. This population included all patients who were eligible for the study, gave their informed consent, returned the patient questionnaire, whose physician returned the physician questionnaire and who had current lipid profile data. Analysis of the physician questionnaire was based on the returned questionnaires.

The main demographic and disease-related data are shown in the table below.

Main demographic and disorder-related data

		PPS N=7281
Age (years)	N	7276
	Mean (SD)	61.0 (11.4)
Gender		
Male	N (%)	4049 (55.6)
Female	N (%)	3231 (44.4)
CHD risk factors		
Cigarette smoking	N (%)	1575 (21.6)
Hypertension	N (%)	6119 (84.1)
Low HDL-C	N (%)	2107 (30.4)
Family history of premature CHD	N (%)	2060 (28.3)
Age (men \geq 45 years; women \geq 55 years)	N (%)	6216 (86.0)
High HDL-C (negative risk factor)	N (%)	600 (8.7)
CHD or CHD risk equivalents		
CHD	N (%)	3448 (47.6)
PAD	N (%)	291 (4.0)
CAD	N (%)	405 (5.6)
Abdominal aortic aneurysm	N (%)	54 (0.8)
Diabetes	N (%)	3205 (44.4)
Multiple risk factors with 10-yr risk for CHD > 20%	N (%)	1401 (20.2)
Metabolic syndrome	N (%)	4411 (61.4)
LDL-C goal according to 2004 updated NCEP ATP III		
<70 mg/dL	N (%)	3557 (49.1)
<100 mg/dL	N (%)	2325 (32.1)
<130 mg/dL	N (%)	1343 (18.5)
<160 mg/dL	N (%)	25 (0.3)
Being on treatment for (years)	N	5908

	Mean (SD)	2.7 (3.0)
Reason of LLD		
Primary prevention	N (%)	3385 (47.6)
Secondary prevention	N (%)	3615 (50.8)
Familial hypercholesterolemia	N (%)	112 (1.6)
Single LLD therapy	N (%)	6594 (90.8)
Statins monotherapy	N (%)	6196 (85.3)
Fibrates monotherapy	N (%)	375 (5.2)
Other monotherapy	N (%)	23 (0.3)
Multiple LLD therapy	N (%)	671 (9.2)

Percentages and summary statistics are based on patients in PPS with non-missing data
 CHD = Coronary heart disease; PAD = Peripheral arterial disease; CAD = Carotid artery disease.

Efficacy results

Patients attaining the LDL-C goals according to the 2004 updated NCEP ATP III guidelines

The percentage of patients attaining the LDL-C goals recommended by the 2004 updated NCEP ATP III guidelines was analysed among those patients within the PPS population with non-missing data.

The percentages of patients reaching the LDL-C goals are presented in in the table below.

Patients attaining the LDL-C goals recommended by the 2004 updated NCEP ATP III guidelines

		Patients on target N (%)
Overall		3576 (49.1)
Country	Korea	818 (51.4)
	Thailand	446 (52.7)
	Taiwan	495 (49.5)
	Indonesia	261 (31.3)
	Philippines	405 (48.6)
	Malaysia	346 (45.1)
	Hong Kong	465 (82.9)
	Vietnam	340 (40.1)
2004 updated NCEP ATP III-recommended LDL-C goals	<70 mg/dL	1240 (34.9)
	<100 mg/dL	1286 (55.4)
	<130 mg/dL	1012 (75.4)
	<160 mg/dL	19 (76.0)
Type of LLD therapy	Statin monotherapy	3151 (50.9)
	Fibrate monotherapy	125 (33.3)
	Other monotherapy	7 (30.4)
	Combination therapy	288 (43.0)
Type of prevention	Primary prevention	1731 (51.2)
	Secondary prevention (after a cardiovascular event)	1759 (48.7)
Metabolic syndrome	Yes	1631 (58.8)
	No	1907 (43.3)

Percentages are based on the number of patients in PPS with non-missing data.

Factors significantly associated with the achievement of 2004 updated NCEP ATP III-recommended LDL-C goals

When adjusted for other factors that proved to be significant ($p < 0.10$) in the univariate analysis, the following patient factors were found to be significantly ($p < 0.01$) associated with the achievement of LDL-C goals in the multivariate analysis:

- LDL-C goal; the chance of reaching the LDL-C goals recommended by the 2004 updated NCEP ATP III guidelines increased with decreasing cardiovascular risk. The odds ratio of reaching the LDL-C goals was 6.25 (95% CI 5.05–7.74) for patients with a LDL-C goal of < 100 mg/dL, 24.56 (95% CI 17.71–34.06) for patients with a LDL-C goal of < 130 mg/dL and 89.33 (95% CI 4.78–1669.52) for patients with a LDL-C goal of < 160 mg/dL when compared with patients with a LDL-C goal of < 70 mg/dL.
- Total cholesterol (TC) level before drug treatment; higher TC level before drug treatment was associated with lower LDL-C goal achievement. For every 100 mg/dL increase in TC level before drug treatment, the odds ratio of reaching the LDL-C goals was 0.67 (95% CI 0.55–0.82).
- Compared with Rosuvastatin monotherapy, odds ratio for other statin treatments or combination treatments in reaching LDL-C goals varied from 0.18 to 0.68.
- Country of residence; when compared with patients in Korea, patients in Malaysia (odds ratio = 0.66; 95% CI 0.44–0.98) and patients in Indonesia (odds ratio = 0.30; 95% CI 0.21–0.43) had lower chances of achieving their LDL-C goals while patients in Hong Kong had a higher chance (odds ratio = 13.06; 95% CI 6.79–25.12) of achieving their goals.
- Therapy compliance; patients with better compliance (who disagreed that they sometimes forget to take their tablets) had a higher chance (odds ratio = 1.49; 95% CI 1.27–1.76) to achieve their goals compared with patients with poorer compliance (who agreed that they sometimes forget to take them). In addition, patients with poorer compliance (who disagreed that they always take their tablets daily to lower cholesterol) had a lower chance (odds ratio = 0.67; 95% CI 0.50–0.89) to achieve their goals compared with patients with better compliance (who agreed that they always take them daily).
- LDL-C level before drug treatment; higher LDL-C level before drug treatment was associated with lower chance of achieving LDL-C goals. For every 100 mg/dL increase in LDL-C level before drug treatment, the odds ratio of reaching the LDL-C goals was 0.46 (95% CI 0.36–0.59).
- Age; higher age was associated with greater chance of achieving LDL-C goals. For every 10-year increase in age, the odds ratio of reaching the LDL-C goals was 1.13 (95% CI 1.05–1.22).
- Systolic blood pressure level; higher systolic blood pressure was associated with lower chance of achieving LDL-C goals. For every 10 mmHg increase in systolic blood pressure level, the odds ratio of reaching the LDL-C goals was 0.94 (95% CI 0.89–0.98).

Due to strong correlation between “country of residence” and “physician’s specialisation”, “physician’s specialisation” was not chosen in the model selection process despite being a significant univariate factor. However, some part of the effect of country of residence may be ascribed to the effect of physician’s specialisation.

Factors significantly associated with allocation to statins

When adjusted for other factors that proved to be significant ($p < 0.10$) in the univariate analysis, the following factors were found to be significantly ($p < 0.01$) associated with allocation to statins in the multivariate analysis:

- Patient's triglycerides (TG) level before drug treatment; higher TG level before drug treatment was associated with less likelihood of being allocated to statin therapy. The likelihood of being allocated to statins was reduced by 3.03-fold (odds ratio = 0.33; 95% CI 0.18–0.61) for patients with TG level before drug treatment between 150 to 199 mg/dL, by 6.25-fold (odds ratio = 0.16; 95% CI 0.09–0.29) for patients with TG level between 200 to 249 mg/dL, by 7.69-fold (odds ratio = 0.13; 95% CI 0.07–0.26) for patients with TG level between 250 to 299 mg/dL and by 20.00-fold (odds ratio = 0.05; 95% CI 0.03–0.08) for patients with TG level ≥ 300 mg/dL when compared with patients with TG level before drug treatment < 150 mg/dL.
- Patient's LDL-C level before drug treatment; higher LDL level before drug treatment was associated with higher likelihood of being allocated to statin therapy. The chance to be allocated to a statin treatment regimen was increased by 3.78-fold (95% CI 2.59–5.53) for patients with LDL-C level before drug treatment ≥ 120 mg/dL when compared with patients with LDL-C level before drug treatment < 120 mg/dL.
- Patient having a history of CHD; the chance to be allocated to statins was increased by 3.24-fold (95% CI 2.05–5.10) for patients with history of CHD when compared with patients without history of CHD.
- Percentage of patients whose recommended treatment is statins (as estimated by physicians); Increase in the percentage by 10%, increases the chance of patients being allocated to statins by 1.39-fold (95% CI 1.20–1.61).

Association between follow-up plan and patient determinants

Due to the small sample size of some of the categories and the absence of statistical tests, the findings in this chapter should be seen as suggestive rather than conclusive.

Overall, among patients who were not at treatment goal and had valid data ($n=2424$), the most frequently allocated follow-up plan was “maintain current treatment” ($n=871$; 35.9%), followed by “increase dosage of current medication” ($n=618$; 25.5%), “switch of medication” ($n=407$; 16.8%) and “lifestyle modification” ($n=332$; 13.7%). Around 6% of patients ($n=156$; 6.4%) were allocated a combination of “switch of medication” and “increase of dosage of current medication” as their follow-up plan while 40 patients (1.7%) were allocated other follow-up plan.

Patient factors which appeared to show an association with the follow-up plan were:

- Country of residence; “switch of medication” tended to have higher percentage of patients in Vietnam ($n=138$; 49.8%) than patients in other countries (0.0–23.8%) while “increase dosage of current medication” tended to have higher percentage of patients in Hong Kong ($n=93$; 100.0%) than patients in other countries (9.0–60.7%). “Combination of switch of medication and increase dosage of current medication”, “lifestyle modification” and “maintain current treatment” tended to have higher percentage of patients in Malaysia ($n=61$; 30.8%), Korea ($n=212$; 27.4%) and Taiwan ($n=270$; 64.0%) respectively.
- Age; patients allocated “switch of medication” or a combination of “switch of medication” and “increase dosage of current medication” tended to be younger while patients allocated “lifestyle modification” or “maintain current treatment” tended to be older. The percentage of

patients allocated “switch of medication” or a combination of “switch of medication” and “increase dosage of current medication” showed a decreasing trend with age, from 23.6% and 18.2% respectively (for <40 years) to 15.3% and 3.3% respectively (for ≥70 years). Conversely, patients allocated “maintain current treatment” or “lifestyle modification” showed an opposite trend, from 23.6% and 5.5% respectively (for <40 years) to 43.1% and 13.1% respectively (for ≥70 years).

- Having a history of CHD; “maintain current treatment” tended to have higher percentage of patients with history of CHD (n=575; 41.5%) than patients without history of CHD (n=296; 28.7%).
- Having a history of CAD; “maintain current treatment” tended to have higher percentage of patients with history of CAD (n=76; 53.1%) than patients without history of CAD (n=792; 35.0%).
- LDL-C goal; patients allocated “switch of medication”, “increase dosage of current medication” or a combination of both tended to have higher LDL-C goal levels while patient allocated “lifestyle modification” or “maintain current treatment” tended to have lower LDL-C goal levels. The percentage of patients allocated “switch of medication”, “increasing dosage of current medication” or a combination of both showed an increasing trend with higher LDL-C goal, from 14.5%, 24.1% and 5.1% respectively (for LDL-C goal <70 mg/dL) to 22.0%, 35.8% and 11.3% respectively (for LDL-C goal <130 mg/dL). Conversely, patients allocated “lifestyle modification” or “maintain current treatment” showed an opposite trend, from 14.5% and 40.7% respectively (for LDL-C <70 mg/dL) to 5.7% and 23.3% respectively (for LDL-C goal <130 mg/dL).
- Type of therapy; patients allocated “switch of medication” or a combination of “switch of medication” and “increase dosage of current medication” tended to be more frequently prescribed fibrate monotherapy (26.5% and 20.4% respectively) than statin monotherapy (16.3% and 5.1% respectively) or combination therapy (14.0% and 9.5% respectively) while patients allocated “increase dosage of current medication” tended to be more frequently prescribed statin monotherapy (28.0%) and patients allocated “maintain current therapy” tended to be more frequently prescribed statin monotherapy (35.8%) or combination therapy (41.6%).
- Unawareness about LDL-C or HDL-C; “maintain current treatment” tended to have higher percentage of patients who were unaware of LDL-C (n=298; 46.8%) or HDL-C (n=306; 45.7%) than patients who were aware of LDL-C (n=413; 28.3%) or HDL-C (n=393; 28.3%)
- Not being given a target cholesterol level; “maintain current treatment” tended to have higher percentage of patients who had not been given a target cholesterol (n=267; 41.8%) than patients who had been given a target cholesterol level (n=338; 28.5%).
- Still on the same tablet but dose has increased since first prescription; “increase dosage of current medication” tended to have higher percentage of patients who indicated that they were still on the same tablet but the dose has increased since first prescription (n=88; 41.7%) than patients who indicated that they were still on the same tablet (n=373; 25.3%) or they have changed their tablets (once: n=63; 11.0% and several times: n=13; 13.5%).
- Not satisfied with the level of information available to them about high cholesterol; “maintain current treatment” tended to have higher percentage of patients who were not satisfied with the

level of information available to them about high cholesterol (n=139; 47.6%) than patients who were satisfied (n=545; 32.1%).

- Frequency of forgetting to take tablets; “maintain current treatment” tended to have higher percentage of patients who forgot to take their tablet no more often than once a month (n=255; 40.3%) than patients who forgot to take their tablet more often than once a month (23.8–26.7%).
- Concerned about the way high cholesterol is treated; “increase dosage of current medication” tended to have higher percentage of patients who were concerned about the way high cholesterol is treated (n=280; 44.1%) while “maintain current treatment” tended to have higher percentage of patients who were not concerned (n=632; 41.8%).

Patient questionnaire

Data presented here were calculated based on the total number of patients in PPS with non-missing data. These data are representative of all the survey countries.

According to patients:

- 68.3% (n=4951) of them had been informed about their cholesterol levels.
- The physician had given a target cholesterol level to 70.0% (n=3925) of them.
- Since being first prescribed a lipid-lowering drug (LLD), about 60% (n=4562; 64.1%) of them were still taking the same drug at the same dose, 8.5% (n=607) had their dose increased by their physician, 23.9% (n=1702) had their drug changed once or twice and 3.5% (n=246) had their drug changed several times.
- When asked about the frequency with which they were seen by the physician for a check-up of their cholesterol, 39.8% (n=2868) indicated to have one check-up every three months, 24.2% (n=1744) had more than one check-up every three months, 21.1% (n=1519) had one every six months, , 8.2% (n=590) had one every year, 2.6% (n=190) had a check-up less often than once a year and 0.9% (n=65) did not have any check-up at all.
- When asked about how often they forgot to take their tablets, 47.8% (n=1942) indicated no more often than once a month, 22.7% (n=925) once every two weeks, 15.6% (n=634) more than once a week and 13.9% (n=566) once a week.
- 46.0% (n=3163) thought that missing a tablet no more often than once a month would not jeopardise their cholesterol levels, 24.9% (n=1708) thought that it was more often than once a week, 20.2% (n=1388) thought that it was once every two weeks, and 8.9% (n=611) once a week.
- Most of them felt satisfied (n=5803; 84.5%) or motivated (n=4828; 75.1%) about the way their cholesterol was being treated.

Physician questionnaire

A total of 501 physicians answered at least one question in the physician questionnaire and returned it. Data presented here were calculated based on the returned number of answers for each question within the physician questionnaire. Most of the physicians were male (n=324; 65.2%). Nearly half (n=238; 48.3%) of the physicians were cardiologists while 32.3% (n=159) were GPs/PCPs, 6.7% (n=33) were endocrinologists and 12.8% (n=63) were of other specialisations. The mean number of years of practice was 16.9 ± 9.1 years.

According to physicians:

- They provided a target cholesterol level to $68.7 \pm 30.0\%$ of their patients.
- Most of them (n=457; 92.7%) used lipid-lowering guidelines to establish individual target cholesterol levels.
- The lipid-lowering guidelines used were: NCEP ATP III guidelines (FRAMINGHAM) (n=331; 83.6%), national guidelines (n=137; 34.6%), the Joint European guidelines (SCORE) (n=52; 13.1%), local healthcare authority guidelines (n=41; 10.4%) and individual practice guidelines (n=29; 7.3%).
- Almost all of them (n=493; 99.0%) had informed their patients of their cholesterol levels when they were first diagnosed with hypercholesterolemia.
- The LLD most frequently recommended to patients was statins ($80.4 \pm 14.6\%$), followed by fibrates ($16.7 \pm 13.0\%$).
- Most of them reported to schedule a visit for reviewing cholesterol levels once every three months (n=198; 40.7%), once every six months (n=126; 25.9%) or more often than once every three months (n=108; 22.2%), while only 9.5% (n=46) scheduled a visit once a year and 1.6% (n=8) scheduled it less often than once a year.
- $52.7 \pm 23.4\%$ of the patients achieved their target level and stayed at this level, while $19.7 \pm 13.5\%$ generally stayed at their target level but sometimes their cholesterol concentration gets too high, $18.5 \pm 14.8\%$ reached their target level in the past but have since relapsed and $9.1 \pm 10.7\%$ had never reached their target level.
- When asked if they agreed that a sufficient number of patients reach their target level, 67.5% (n=337) of them agreed or strongly agreed with that, 22.2% (n=111) had neutral feelings and 10.2% (n=51) disagreed or strongly disagreed.