



STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not applicable

ACTIVE INGREDIENT: Not applicable

Study No: NIS-CTR-XXX-2012/1

**Observational study to understand patients' and physicians'
attitudes to STatins in TurkeY**

STAY Study

Developmental Phase: Not applicable

Study Completion Date: 31 Jan 2013(DBL)

Date of Report: 17 Dec 2013

OBJECTIVES:

Primary:

- To assess patients' and physicians' attitudes to statins by mean of HABIT Patient and Physician survey respectively.

Secondary:

- To assess factors associated to different results on the HABIT assessment tool (socio-demographic, clinical, etc).
- To describe the use of statins in patients with hypercholesterolemia in Turkey.
- To compare real-life patterns of statins use with current guidelines available in Turkey to assess the degree of concordance.

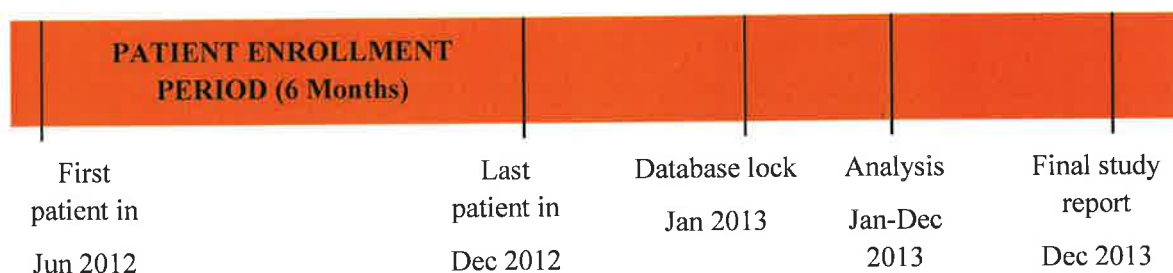
METHODS:

Study Design and Flow Chart

This is a national, multi-center, cross-sectional study conducted in 14 centers in Turkey. Patients >18 years of age, diagnosed with hypercholesterolemia according to ICD-10 and prescribed with at least one statin irrespective of its type and/or dose were planned to be invited to participate in the study. All patients with hypercholesterolemia, attending the participating centers during the 6 month enrolment period (between June - December 2013) and who met the subject selection criteria were candidates to participate in the study. There was no pre-determined method for subject selection, and subjects who meet the inclusion criteria were invited to the study based on their admittance order.

In this multi-center, cross-sectional observational study, no diagnosis or follow-up processes were defined except the routines; there is no intervention to the physicians' treatment choices and treatment change was not required. There was not investigational product.

Figure 1 Study Flow Chart



The following information was obtained directly from the subject and through the medical records of the subject at the only study visit.

1. Subject and disease characteristics:
 - a) Demographic characteristics: age, gender, educational status, occupation, place of living, income status.
 - b) Physical examination findings: height, weight, waist circumference, blood pressure, pulse.
 - c) Presence of cardiovascular risk factors (hypertension, atherosclerosis, peripheral arterial disease, abdominal aortic aneurysm, sympathetic carotid artery disease, smoking, diabetes mellitus, diet, exercise etc.).
 - d) Co-morbid diseases (coronary arterial disease, stroke, transient ischemic attack, cardiovascular disease history, etc.)
 - e) Concomitant treatments.
 - f) Blood lipid parameters (prior to statin treatment, after discontinuation of treatment and current) (Will be recorded if available).

- g) Other laboratory parameters (plasma glucose level, hepatic and muscular enzymes, etc.) (Will be recorded if available).
2. Information on hypercholesterolemia treatment
 - a) Information on the statin treatment used: duration of use in the past one year
 - b) Other treatments used for hypercholesterolemia treatment in addition to statin therapy (ezetimibe, fibrate, niacin, etc.)
 - c) Non-medication methods recommended in addition to statin treatment (dietary recommendations, life style changes, support for smoking cessation in case of smoking, information brochure, meeting invitation, training, etc.)
 - d) Information on physician who initiated statin treatment and the hospital where he/she works (speciality of the physician (general practitioner, primary care, internal medicine specialist, cardiologist, etc.), type of the hospital (private hospital, state hospital, university hospital), healthcare coverage systems applicable at the hospital (Social Security Institution, private insurance).
 3. Information on discontinuation of statin treatment
 - a) Information on the person who discontinues statin treatment (the subject, physician recommending statin treatment, another physician)
 - b) Reasons to discontinue statin treatment (lack of efficacy, normalization of lipid parameters, concern of adverse events, occurrence of adverse event, difficulty in obtaining the drug (inability to obtain a report, high price), obtaining unfavorable information about the drug, conception of decreasing high cholesterol levels as necessary, etc.)
 - c) Medications and non-medication therapies used for treatment of hypercholesterolemia following discontinuation of statin treatment (dietary habits, exercise schedule, training meeting, telephone visits, herbal treatments, etc.)
 4. The patient will be asked to answer the HABIT Questionnaire for Patients.

Inclusion/Exclusion Criteria:

Patients needed to fulfill the following criteria to be involved in this study:

1. Provision of subject informed consent
2. Female and/or male aged over 18 years
3. Clinical diagnosis of hypercholesterolemia according to ICD-10 classification
4. Receiving at least one prescription of one statin during the last 6 months.
5. To be an outpatient

The prescription of the medicinal product was clearly separated from the decision to include the subject in the NIS.

Patients fulfilled at least one of the following criteria were excluded:

- Pregnant women
- Patients unable to read and/or understand the study questionnaires
- Receiving statin at the time of admittance
- Patients participating in randomized clinical trials
- Patients included in this study once

RESULTS:

Patient profile:

Mean (SD) age of the patients included in the study was 57.4 (11.5) years and 55.5% was <60 years of age. Of all patients, 47.6% was males; 62.6% had received primary school education or below; and most of them (81.6%) was living at urban sites. Total annual income of the family was <20,000 TL for 66.2% of the patients; 43.2% had no current job and no retirement pension. However, 99.1% of them had some kind of health insurance.

In 321 patients (60.3%), there was comorbidit(y)ies together with hypercholesterolemia. The most three frequent of these comorbidities were hypertension, diabetes and coronary heart disease.

Mean (SD) of anthropometric measurements and vital signs were as follows: Height 165.9 (8.7) cm; body weight 80.4 (14.9) kg; waist circumference for females 98.4 (16.7) and males 98.3 (12.1) cm; pulse 77.0 (10.8) beat per minute; systolic and diastolic blood pressure 135.2 (19.9) and 83.3 (12.4) mmHg.

At the time of the study visit, mean (SD) total cholesterol level was 235.8 (50.6), LDL-cholesterol 159.8 (44.7), HDL-cholesterol 45.1 (11.6) and triglyceride 195.5 (114.3) mg/dL. When those levels were compared with those at the beginning and discontinuation times of statin treatment, it was seen that total cholesterol, LDL-cholesterol and triglyceride levels had significantly decreased with the initiation of statin treatment, but had returned to the previous levels with the discontinuation.

The most frequent cardiovascular risk factors among the study patients were high cholesterol levels (83.1%), hypertension (67.7%) and physical inactivity (67.1%); followed by high triglyceride, diabetes and coronary heart disease in almost half. Obesity and smoking were relatively less (35.5% and 26.5%).

In 480 patients with a known duration of hypercholesterolemia, mean (SD) time after diagnosis was 4.9 (4.2) (median 3.9, minimum and maximum 0.06-23.96) years.

It was recorded that 52.4% of the patients were on concomitant medications. A small number of patients were using other lipid lowering drugs in combination of statins, but use of non-drug product use was more frequent.

APPROACH TO STATIN TREATMENT:

HABIT questionnaire

Upon patient HABIT questionnaire:

- Most of the patients said that they had no or negative idea about the efficacy of lipid lowering drugs (mean [min-max] score 0 [(-4)-(+4)]).

- Most of the patients did not have an idea or have an incorrect information about the association between adverse events and dosage of the lipid lowering drugs (median [min-max] score 0 [(-7)-(+8)]).
- Approximately 30% of the patients were not aware of the risk of having high cholesterol levels (median [min-max] score 0 [(-3)-(+4)]).
- Most of the patients, although they seemed to be aware of risks of hypercholesterolemia, were not aware of its importance (median [min-max] score 1 [(-8)-(+8)]).
- A marked fraction of the patients were not aware of the necessity of patients' treatment compliance; but knew that they could prevent the need of drug dose increase (median [min-max] score 0 [(-4)-(+4)]).
- However, approximately half of the patients declared that they had difficulty in applying the doctor's recommendations (median [min-max] score 1 [(-6)-(+6)]).
- The patients who were positive towards his/her communication with their doctor were in the majority, but 30% had negative perception (median [min-max] score 3 [(-6)-(+6)]).
- The majority (approximately 60%) stated that his/her doctor informed him/her about cholesterol most of the time / always; however, 40% of them thought negative (median [min-max] score 5 [(-12)-(+12)]).

Upon physician HABIT questionnaire:

- The majority was thinking positively about the efficacy of the statins (median [min-max] score -1 [(-3)-(+3)]).
- The majority was thinking that dose titration was not perceived negatively by the patients (median [min-max] score -2 [(-4)-(+2)]).
- Almost all believed that patients might not high statin doses; that high doses should be used carefully, but close follow-up of most patients using high dose statins might not be possible; that higher LDL decrease would be provided by higher doses and patients would both be against dose increase (median [min-max] score -1 [(-6)-(+9)]).
- The physicians declared various ideas about achieving and values of LDL targets (median [min-max] score -2 [(-6)-(+4)]).
- Of 25-49%, they were considering achieving cholesterol goals were of secondary importance (median [min-max] score -2 [(-4)-(+3)]).
- The majority thought that patients showed poor compliance to non-drug treatment options so that waiting to see the results of those approaches would delay drug treatment (median [min-max] score 3 [(-6)-(+8)]).

- Approximately half of the physicians were thinking that they reserve enough guidance to their patients (median [min-max] score 3 [(-5)-(+8)]).
- Seventy five %75 was thinking that measures to be taken to achieve cholesterol goal was under his/her control, however, only half of them were able to reserve enough time and resources for their patients for this goal; but despite this, almost all of them were content with their patients' ability reaching the cholesterol goals (median [min-max] score 3 [(-3)-(+7)]).

When the impact of sociodemographic and clinical characteristics of the patients on HABIT scores was investigated, the following findings were obtained:

Patient age, classified as <60 and ≥60 years, had significant impact on several items:

In ≥60 years age group,

- negative perception of efficacy of cholesterol lowering drugs were more frequent (p=0.007);
- negative idea of the impact of decreasing cholesterol levels would prevent heart attack or other cardiac problems in the long run was more frequent (p=0.028);
- perception that “people without heart attack or other cardiac problem history would not have concerns about their cholesterol levels” was more frequent (p=0.022);
- there was a higher percentage of negative thinking of their physicians communication with them (p=0.001; 0.017; 0.002);
- higher percentage was thinking that their doctor in giving insufficient information about cholesterol related issues (p<0.001 – 0.002).

Linear regression model revealed and between HABIT scores and age: “HABIT score=15.596 - (0.131 x age (years))” so that if age is known, HABIT score might be predicted with the above formula.

When the patients were classified according to educational status as ≤ primary school and ≥high school; educational status had significant impact on several issues as summarized below:

In patients received ≤ primary school education:

- there were thinking more negative of cholesterol lowering drugs' efficacy (p=0.022);
- little concern was detected about the association of high doses and adverse drug reactions (p<0.001 – 0.017);
- a higher percentage had negative idea about that the risk of heart attack among people with high cholesterol levels was higher compared to those with lower cholesterol, and that decreasing cholesterol levels might decrease the future risk of heart attack or other cardiac problems (p<0.001 and p=0.001);
- a lower belief in the idea that people may prevent dose increase of lipid lowering drugs buy low cholesterol / low fat containing diet and appropriate exercise (p=0.003);

- the percentage of patients who found exercising 3 times a week difficult was higher (p=0.033);
- the percentage of patients who thought than his/her doctor was listening him/her all the time was lower (p=0.022);
- The percentage of the patients who thought that their doctor gave insufficient information about cholesterol was higher (p<0.001).

There was no significant influence of the duration of hypercholesterolemia when classified as < and \geq 1 year, on HABIT scores.

Total HABIT scores of patients with a waist circumference higher than normal were significantly lower as well as the sub-scores of items related to the importance of high cholesterol and communication by their physician about cholesterol related issues.

High blood pressure patients had significantly lower HABIT sub-scores about the association of high doses with adverse drug reactions, risk of high cholesterol level, and difficulty to apply the advices / recommendations.

The presence of comorbidities had significant impact on many sub-scores.

Apart from HABIT scores, the impact of clinical features on HABIT questions when interpreted in detail revealed that the increase in disease duration has a negative impact of doctor-patient communication; waist circumference, blood pressure and comorbidities did not have a consistent influence on HABIT responses even if the relationships were statistically significant.

Reasons of discontinuation of statin treatment:

Half (55.8%) of the doctors who had initiated statin treatment was cardiologists while 29.1% was internal medicine specialists and only 1.7% family physicians. They were mostly (64.7%) working at state hospitals while 19.5% was at the university hospitals.

The patients had used statins for a mean(SD) of 3.8 (3.9) years; while this duration was significantly longer among ≥ 60 year-olds (p=0.07); no effect of education status on statin use duration could have been found.

Of non-drug treatment options, diet modifications (%61.3) and physical exercise (%56.8) were the most frequent.

The discontinuation decision of statin treatment was given by the patient themselves in 73.7% of the cases. The most frequent three reasons of discontinuation were “negative impressions / news about statin in general (%40)”, “negative impressions / news about statin on TV programs (32.9%)” and “insufficient information about high cholesterol and its risks (30.6%)”. Those negative impressions / news / programs were about side effects of statins regarding the liver (38.0%), kidneys (33.8%) and skeletal muscle (32.9%). Low access due to prices was a rare reason (%2.4).