AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: CRESTOR®
ACTIVE INGREDIENT: rosuvastatin

Study No: NIS-CSI-CRE-2006/1, NCT 00837083
Evaluation of Crestor® (rosuvastatin) in daily practice

Developmental phase: Post-marketing non-interventional study
Study Completion Date: October 2007
Date of Report: 15 July 2008

OBJECTIVES:

The present study has been designed to answer the following questions:

1. What is the effectiveness of 10 mg rosuvastatin in high-risk patients in daily practice?
2. What proportion of patients achieve target LDL-cholesterol levels using the initial rosuvastatin dose?
3. How safe is rosuvastatin therapy?
4. How reliably are patients taking the drug?
5. Whati is the influence of rosuvastatin on the AST, ALT and CK levels?

METHODS:

This trial was a prospective, non-randomised, non-interventional follow-up clinical study. The study included 602 patients with hypercholesterolaemia and 10-year cardiovascular complications risk of at least 20% or a pre-existing atherosclerotic disease, for whom 10 mg rosuvastatin was considered the most appropriate therapy by the treating physician. Administration of any other therapy in the study was based on physicians' clinical decision and according to the current professional guidelines. Patients who have adhered to the recommended dyslipidaemia management dietary guidelines for at least 12 weeks, attended two clinical visits at an interval of at least 12 weeks. At Visit 1 (baseline visit) blood samples were taken for laboratory tests (total cholesterol, HDL-cholesterol, triglycerides, AST, ALT, CK levels); height, weight, waist circumference and blood pressure were measured; and smoking status was assessed. At Visit 1 rosuvastatin was prescribed and the quantity of prescribed tablets was noted.

At Visit 2 (final visit) that took place at least 12 weeks later, blood samples were taken for laboratory tests and the same parameters were measured as at Visit 1. At Visit 2, number of used rosuvastatin tablets as well as the time from the beginning of rosuvastatin use till Visit 2 were recorded.
The extent of rosuvastatin effect on liver enzymes was assessed using the following criteria:

Normal value	≤ upper limit of normal (ULN)
Mild elevation	> ULN and ≤ 2x ULN
Moderate elevation	> 2x ULN and ≤ 3x ULN
Relevant elevation	> 3x ULN and ≤ 4x ULN
Clinically relevant elevation	> 4x ULN

Ninety eight (98) physicians with a specialty in family medicine or internal medicine participated as investigators in the study.

RESULTS:

Data for all study subjects

The study included 602 subjects (332 men [55%] and 265 women [44%]). Data on gender were missing for 5 subjects (1%). The mean age of patients in the study was 60.4 years (standard deviation [SD] ± 10.4 years) and the mean height was 168.9 cm (SD ± 8.9 cm). 157 (26%) patients had diabetes (3 patients Type 1, 142 patients Type 2), 200 (33%) had coronary artery disease, and 328 (54%) had other conditions. 310 (51%) subjects in the University Clinical Centre Ljubljana [UCCL] subgroup had a family history of dyslipidaemia or early coronary artery disease. Basic characteristics of study subjects are presented in Table 1. Table 2 shows mean serum lipid levels, Table 3 liver transaminases and creatinine-phosphokinase levels at Visit 1 and Visit 2 (excluding subjects enrolled in the UCCL), and Table 4 shows data on severity and relevance of liver transaminases and creatinine-phosphokinase elevations (excluding subjects enrolled in the UCCL).

Table 1: Severity of some risk factors for the overall study population (BMI = Body Mass Index)

	Visit 1	Visit 2
Mean body weight (kg)	81.5 ± 13.5	80.6 ± 13.3
Mean waist circumference	97.6 ± 10.9	96.7 ± 10.6
Mean Body Mass Index (kg/m^2)	28.5 ± 3.9	28.2 ± 3.9
Number of patients with BMI < 25 kg/m^2	103	124
Number of patients with BMI < 25 kg/m^2	277	237
Number of patients with BMI < 30 kg/m^2	211	154
Mean systolic blood pressure (mmHg)	142.9 ± 19.3	135.5 ± 14.2
Mean diastolic blood pressure (mmHg)	85.9 ± 10.8	82.7 ± 8.3
Smokers – number (%)	174 (29%)	131 (22%)

Table 2: Mean serum lipid levels (in mmol/L) at Visit 1 and Visit 2

	Visit 1	Visit 2	Difference (%)	p
Total cholesterol	6.9 ± 1.2	4.8 ± 1.1		
HDL	1.3 ± 0.5	1.3 ± 0.4		
LDL	4.3 ± 1.1	2.8 ± 0.9		
Triglycerides	2.5 ± 1.9	1.8 ± 1.1		

Table 3: Mean values (with standard deviation and coefficient of variation) of liver enzyme and creatinine-phosphokinase at Visit 1 (1) and Visit 2 (2) by gender (excluding subjects enrolled in the UCCL)

		AST		ALT		CPK	
		1	2	1	2	1	2
Men	Mean value	0.47	0.49	0.57	0.61	1.78	1.84
	Standard deviation	0.17	0.18	0.24	0.28	1.04	0.81
	Coefficient of variation	36.0%	37.2%	42.6%	46.0%	58.8%	44.1%
Women	Mean value	0.40	0.44	0.45	0.45	1.40	1.70
	Standard deviation	0.17	0.42	0.18	0.19	1.42	1.04
	Coefficient of variation	41.5%	95.2%	39.5%	41.7%	58.8%	61.1%

Table 4: Number (and %) of patients with missing data for normal/elevated serum liver transaminase and creatinine-phosphokinase levels at Visit 1 (1) and Visit (2) (excluding subjects enrolled in the UCCL)

	AST		ALT		CK	
	1	2	1	2	1	2
Not available	193	193	180	186	292	273
Normal level	217 (83%)	208 (80%)	215 (78%)	200 (75%)	149 (92%)	162 (90%)
Mild elevation	42 (16%)	51 (20%)	59 (22%)	66 (25%)	12 (7%)	17 (9%)
Moderate elevation	2 (1%)	1 (<1%)	0 (0%)	2 (0%)	1 (<1%)	2 (1%)
Relevant elevation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Clinically relevant elevation	0 (0%)	1 (<1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Data on subjects enrolled in the UCCL

The study included 148 subjects (80 [54%] men, 64 [43%] women) enrolled by investigators in the University Clinical Centre Ljubljana (UCCL). Data on gender were missing for 4 subjects (3%). The mean age of patients in this subgroup was 61.2 years (standard deviation [SD] ± 11.1 years) and the mean height was 169.5 cm (SD ± 9.7 cm). 41 (28%) patients had diabetes (39 [95%] Type 2, data on diabetes type are missing for 2 patients [5%]), 75 (51%) patients had coronary artery disease, and 85 (57%) had other conditions. 55 (37%) subjects in the UCCL subgroup had a family history of dyslipidaemia or early coronary artery disease. Basic characteristics of the UCCL subgroup are presented in Table 5. Table 6 shows mean serum lipid levels, Table 7 mean values (with standard deviation and coefficient of variation) of liver transaminases and creatinine-phosphokinase at Visit 1 and Visit 2 by gender, and Table 8 shows data on severity and relevance of liver transaminases and creatinine-phosphokinase elevations for the subgroup.

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Table 5: Severity of some risk factors for the subgroup of UCCL subjects (BMI = Body Mass Index)

	Visit 1	Visit 2
Mean body weight (kg)	80.3 ± 11.6	79.3 ± 12.0
Mean waist circumference	98.5 ± 9.1	97.2 ± 9.7
Mean Body Mass Index (kg/m^2)	27.9 ± 3.3	27.5 ± 3.3
Number of patients with BMI < 25 kg/m^2	26	29
Number of patients with BMI < 25 kg/m^2	87	82
Number of patients with BMI < 30 kg/m^2	32	26
Mean systolic blood pressure (mmHg)	144.7 ± 19.4	136.7 ± 14.7
Mean diastolic blood pressure (mmHg)	85.6 ± 11.8	82.1 ± 8.5
Smokers – number (%)	40 (27%)	21 (14%)

Table 6: Mean serum lipid levels (in mmol/L) at Visit 1 and Visit 2 for the UCCL subgroup

	Visit 1	Visit 2
Total cholesterol	6.3 ± 1.2	4.5 ± 1.0
HDL	1.2 ± 0.3	1.3 ± 0.3
LDL	4.1 ± 1.1	2.5 ± 0.8
Triglycerides	2.1 ± 1.0	1.5 ± 0.9

Table 7: Mean values (with standard deviation and coefficient of variation) of liver enzyme and creatinine-phosphokinase at Visit 1 (1) and Visit 2 (2) by gender for the UCCL subgroup of patients

		AST		ALT		CPK	
		1	2	1	2	1	2
Men	Mean value	0.56	0.58	0.62	0.67	2.11	1.61
	Standard deviation	0.31	0.23	0.30	0.35	2.52	0.65
	Coefficient of variation	55.7%	39.4%	48.6%	52.9%	119.5%	40.4%
Women	Mean value	0.47	0.49	0.51	0.54	1.23	1.52
	Standard deviation	0.16	0.21	0.22	0.28	0.62	1.05
	Coefficient of variation	34.0%	42.9%	41.9%	51.6%	50.9%	69.3%

Table 8: Number (and %) of patients with missing data for normal/elevated serum liver transaminase and creatinine-phosphokinase levels at Visit 1 (1) and Visit (2) for the UCCL subgroup of patients

	AST		ALT		CK	
	1	2	1	2	1	2
Not available	43	38	42	39	46	48
Normal level	73 (70%)	71 (64%)	75 (71%)	74 (68%)	92 (90%)	94 (94%)
Mild elevation	30 (29%)	35 (32%)	30 (28%)	31 (28%)	7 (7%)	5 (5%)
Moderate elevation	1 (<1%)	4 (4%)	1 (1%)	4 (4%)	1 (1%)	1 (1%)
Relevant elevation	1 (<1%)	0 (0%)	0 (0%)	0 (0%)	1 (<1%)	0 (0%)
Clinically relevant elevation	0 (0%)	0 (<1%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)

Data on compliance with rosuvastatin for all subjects and the UCCL subgroup are shown in Table 9, and changes in 10-year cardiovascular risk are presented in Table 10.

Table 9: Number of prescribed tablets, number of used tablets and the prescribed/used tablets ratio.

	All			University Clinical Center Ljubljana		
	Prescribed tablets (n=527)	Used tablets (n=532)	Prescribed/used tablets ratio (n=527)	Prescribed tablets (n=130)	Used tablets (n=120)	Prescribed/used tablets ratio (n=120)
Mean	86.7	75.9	0.86	91.1	84.8	0.89
Standard deviation	29.0	33.1	0.17	43.6	42.7	0.16
Coefficient of variation	33.4%	43.4%	19.8%	47.8%	50.4%	18.0%

Table 10: Changes in estimated 10-year cardiovascular risk before and after the therapy for all patients and for the UCCL subgroup

	All		University Clinical Center Ljubljana	
	Before therapy (n=545)	After therapy (n=511)	Before therapy (n=111)	After therapy (n=99)
<20%	104 (19%)	240 (47%)	35 (13%)	67 (68%)
20% and over	65 (12%)	31 (6%)	11 (10%)	4 (4%)
20–40%	322 (59 %)	204 (40%)	56 (50%)	22 (22%)
>40%	54 (10%)	36 (7%)	9 (8%)	6 (6%)