Clinical Study Report Synopsis

Drug Substance	Rosuvastatin Calcium
Study Code	DM-CRESTOR-0002 / D3560L00075
Edition Number	2.1
Date	28-March-2010

A double blind, double dummy, phase IV, randomized, multicenter, parallel group, placebo control trial to evaluate the effect of rosuvastatin on triglycerides levels in Mexican hypertriglyceridemic patients.

Study dates:

FIRST SUBJECT ENROLLED: 09 JANUARY 2007

LAST SUBJECT LAST VISIT: 09 FEBRUARY 2009

Phase of development: Therapeutic use (IV)

This study was performed in compliance with Good Clinical Practice, including the archiving of essential documents.

Study centre(s)

12 Centres around Mexico in Mexico City, Toluca, Guadalajara, Monterrey and San Luis Potosí.

Publications

Abstract Presented at the 59th annual meeting of the American College of Cardiologist, 2010

Objectives and criteria for evaluation

Table S1 Primary and secondary objectives and outcome variables

Objectives	Outcome variables	Type
Primary	**Primary**	
Evaluate the efficacy of rosuvastatin in reducing triglycerides levels in hypertriglyceridemic Mexican patients from baseline to week 8	Reduction in triglycerides levels	Efficacy
Secondary	**Secondary**	
To evaluate the efficacy of RSV from baseline to week 8 on: Non-HDL-C levels	Reduction in Non-HDL levels	Efficacy
1. To evaluate the efficacy of RSV from baseline to week 8 on a. Low-density lipoprotein cholesterol (LDL-C) b. Total cholesterol (TC) c. High-density lipoprotein cholesterol (HDL-C) d. Apolipoprotein A1 (ApoA-1), apolipoprotein B (ApoB) and e. TC/HDL-C, LDL-C/HDL-C, nonHDL-C/HDL-C and ApoB/ApoA-1 indexes.	Reduction in LDL-C, TC, Apo B levels Increase in HDL-C and Apo A levels Changes in TC/HDL-C; LDL-C/HDL-C; nonHDL-C/HDL-C levels and ApoB/Apo A indexes.	Efficacy
2. To determine the efficacy of RSV in reducing high-sensitive C- reactive protein (hsCRP) from baseline to week 8.	Reduction in hsCRP levels	Efficacy

Objectives	Outcome variables	Type
4. To evaluate the effect of RSV on the incidence and severity of adverse events and laboratory data	Adverse event reports including laboratory an cabinet alterations	Safety

Study design

This was an 8 week, randomised, double blind, double dummy, national, multicentre study with 3 parallel treatment groups: rosuvastatin 10 mg, rosuvastatin 20 mg and placebo. There where 4 clinic visits: 1 and 2 ocurred during the lead-in-period; 2.1 was the randomisation visit, and V3 was the final visit. All elegible patients were randomised in a 1:1:1 ratio to receive ether rosuvastatin 10 or 20 mg/day or placebo once a day. Patients were followed fo 8 weeks.

Target subject population and sample size

Mexican subjects with hypertriglyceridemia, ≥Approximately 10 to 12 centres will be required in order to recruit 330 randomised patients, of whom 285 to 300 are expected to be fully evaluable (i.e., to allow for approximately 10 to 15% of randomised patients being non-evaluable). Investigational product and comparator(s): dosage, mode of administration and batch numbers

Rosuvastatin 10 milligrams batch number 105461 and rosuvastatin 20 milligrams batch number 105884 were used in this study and compared with placebo matching rosuvastatin 10 milligrams batches number TX27001 and TX17031 and placebo matching rosuvastatin 20 mg batches number TX17029 and TX27002. All investigational products and placebo were given orally once a day.

Duration of treatment

Treatment was given for 8 weeks.

Statistical methods

Subject population

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Summary of efficacy results

334 patients were randomized (Table 1). Here we present the results at eight weeks of treatment of 312 patients (RSV10: 102; RSV20: 107 and PBO: 103).

Table S2 Statistical analysis of changes from baseline to 8 weeks.

	Baseline		Change from baseline			95% CI of change
	Mean	(SD)	Mean	%	(SD)	
Triglycerides levels (mg/dl)						
Rosuvastatin 10 mg	319.51	131.95	-67.95	**-21.27%**	12.78	(-93.31 , -42.59)
Rosuvastatin 20 mg	296.78	95.19	-78.61	**-26.49%**	11.65	(-101.70 , -55.51)
Placebo	309.46	99.55	-22.31	**-7.21%**	11.88	(-45.87 , 1.25)
Non-HDL-C (mg/dl)						
Rosuvastatin 10 mg	179.38	39.22	-52.76	**-29.41%**	48.08	(-62.25 , -43.27)
Rosuvastatin 20 mg	178.88	39.42	-61.31	**-34.27%**	46.63	(-70.29 , -52.33)
Placebo	182.14	34.01	-1.06	**-0.58%**	37.41	(-8.41 , 6.28)
LDL-C (mg/dl)						
Rosuvastatin 10 mg	129.24	28.23	-42.23	**-32.68%**	2.83	(-47.84 , -36.62)
Rosuvastatin 20 mg	130.51	29.19	-53.22	**-40.78%**	3.17	(-59.51 , -46.94)
Placebo	129.77	31.10	2.66	**2.05%**	2.85	(-3.00 , 8.31)
Total Cholesterol (mg/dl)						
Rosuvastatin 10 mg	217.05	37.18	-49.73	**-22.91%**	4.07	(-57.80 , -41.65)
Rosuvastatin 20 mg	215.58	36.71	-63.32	**-29.37%**	4.15	(-71.55 , -55.08)
Placebo	213.68	34.66	1.44	**0.67%**	3.45	(-5.40 , 8.27)
HDL-C (mg/dl)						
Rosuvastatin 10 mg	33.50	7.52	3.49	**10.42%**	7.16	(2.07 , 4.90)
Rosuvastatin 20 mg	34.05	6.88	2.49	**7.31%**	5.78	(1.38 , 3.59)
Placebo	32.30	6.49	1.95	**6.04%**	7.42	(0.50 , 3.40)
ApoA1 levels (mg/dl)						
Rosuvastatin 10 mg	130.06	22.72	4.66	**3.58%**	2.31	(0.06 , 9.25)
Rosuvastatin 20 mg	129.34	19.85	6.79	**5.25%**	1.81	(3.21 , 10.37)
Placebo	124.33	16.73	2.65	**2.13%**	1.92	(-1.16 , 6.46)
ApoB Level (mg/dl)						
Rosuvastatin 10 mg	114.88	20.44	-27.05	**-23.55%**	2.68	(-32.36 , -21.73)
Rosuvastatin 20 mg	114.19	20.88	-36.81	**-32.24%**	2.28	(-41.33 , -32.28)
Placebo	113.61	22.81	1.43	**1.26%**	2.58	(-3.68 , 6.54)
HsCRP (mg/dl)						
Rosuvastatin 10 mg	0.55	1.15	-0.19	**-34.55%**	0.12	(-0.41 , 0.04)

Rosuvastatin 20 mg	0.41	0.39	-0.11	**-26.83%**	0.03	(-0.18 , -0.05)
Placebo	0.46	0.92	0.01	**2.17%**	0.10	(-0.19 , 0.20)

Summary of pharmacokinetic results

NA

Summary of pharmacodynamic results

NA

Summary of pharmacokinetic/pharmacodynamic relationships

NA

Summary of pharmacogenetic results

NA

Summary of safety results

The adverse events frequency by treatment are shown in the table S3

Table S3 Number (%) of patients who had a adverse event in any category, safety analysis set

Category of adverse event	**Safety Analysis Set (N=334)**		
	RSV 10 mg (N=111)	RSV 20 mg (N=112)	Placebo (N=111)
Number of AE			
Any adverse event	27(24.32%)	28(25%)	20(18.02%)
Serious adverse event	0 (0%)	1 (0.89%)	0 (0%)
Causally related SAEs	0 (0%)	0 (0%)	0 (0%)