Clinical Study Results Posting Template

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Posting Results:

☐ Study in patients with a serious or life-threatening disease or condition

☒ Hypothesis-testing study in any indication

☐ Non-interventional study with an approved AZ medicine

1. Titles and Background Information

- Protocol ID: 4522AS/0002
- Secondary ID:
- Official Title: A double-blind, randomised, placebo-controlled, parallel-group, multicentre, phase III study to assess the impact of rosuvastatin treatment for 26 weeks (titrated to a maximum dose of 40mg once daily) on left ventricular function, cytokines and lipid parameters in patients with established systolic chronic heart failure.
- Finished Product: Crestor
- Active Ingredient: rosuvastatin
- Study Phase: Phase III
- Study Status: completed
- Condition/Disease: Ischaemic or non-ischaemic, systolic congestive heart failure

2. Key Study Dates

- Study Start Date: 18 February 2003
- LSLV Date: 8 April 2005

- Database Lock: 1 August 2005
- Approval Date: February 2007

3. Objectives

1. Primary Outcome

   Determine the effect of rosuvastatin (up-titrated to a dose of 40mg/day) compared to placebo on cardiac remodelling, estimated by change in left ventricular ejection fraction on radionuclide ventriculography, at 26 weeks post randomization from baseline.

2. Secondary Outcome

   Determine the effects of rosuvastatin (up-titrated to a dose of 40mg/day) compared to placebo by measuring:

   - Changes from baseline at 26 weeks post-randomisation, of left ventricular (LV) end-diastolic and end-systolic diameter, and LV fraction shortening, as determined by transthoracic echocardiography.
   - The percentage change in lipid parameters: total cholesterol, low density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglycerides after 6, 12 and 26 weeks post-randomisation
   - Changes from baseline at 26 weeks post-randomisation in neurohormonal and immunological markers: norepinephrine, endothelin, N-terminal pro-brain natriuretic peptide, high-sensitivity C-reactive protein, tumour necrosis factor α and interleukin 6.

   Assess the safety of rosuvastatin over 26 weeks determined by the incidence and severity of adverse events and abnormal laboratory values.

Assess change in quality of life score, as determined by the Minnesota Living with Heart Failure questionnaire.

4. Methods

A 6-month randomized placebo (PBO)-controlled study of rosuvastatin (ROS) was conducted in patients with systolic CHF of ischemic or nonischemic etiology. The primary end point was change in LVEF by radionuclide ventriculogram. Secondary end points included change in echocardiographic parameters, neurohormonal and inflammatory markers, Packer composite score, death, and heart failure hospitalization. 131 patients entered into the study of which 86 were randomised and 71 completed.

- Inclusion Criteria:

Signed informed consent, males or females aged 18 or older, LVEF ≤40% assessed by RNVG or contrast ventriculogram or ≤35% assessed by TTE within the previous 6 months, LVEF <45% as assessed by RNVG during Visit 1, NYHA Class II, III or IV symptoms primarily related to heart failure, ischaemic and non-ischaemic patients and on stable heart failure therapy as defined by physician's best practice.

- Exclusion Criteria:

Key exclusion criteria include acute myocarditis within the last 12 months, diabetes mellitus not controlled by diet, oral therapy or insulin therapy, homozygous familial hypercholesterolaemia, receiving biventricular pacing or expected to receive biventricular pacing in the next 6 months, subjects who normally would be considered for statin therapy in the next 6 months, sever hypertension, history of definite myocardial infarction, cerebrovascular accident, percutaneous transluminal coronary angioplasty or coronary bypass graft within 3 months prior to enrolment in the study, body mass index <15, plus others.

5. Results

See publication

6. Reference: Published

Citation: Krum H, Ashton E, Reid C, Kalff V, Rogers J, Amarena J et al. Double-blind, randomized, placebo-controlled study of high-dose HMG Co-A reductase inhibitor therapy on ventricular remodelling, pro-inflammatory cytokines and neurohormonal parameters in patients with chronic systolic heart failure. J Card Fail 2007 Feb; 13(1): 1-7.

PMID: