



## MEMORANDUM

Date: December 1, 2008

Re: **The JUPITER Trial:** *Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin*

To: All Interested Physicians

From: Mary Honkanen, M.D., ABCL, FAHA

The results of the JUPITER Trial, a study evaluating the effect of Crestor on cardiovascular (CV) events in relatively healthy persons with levels of LDL below current treatment thresholds but with elevated levels of high-sensitivity C-reactive protein, were announced at the recent American Heart Association meeting in New Orleans. The results were remarkably positive. The study is in the November 20<sup>th</sup> issue of the NEJM. The press has already given the study a lot of attention, so the following is a summary that may prove helpful if your patients have questions.

- I. The Jupiter Trial: Rosuvastatin (Crestor) to Prevent Vascular Events in Men and Women with Elevated C - Reactive Protein. (Paul M. Ridker et al., NEJM: Vol 359. No 21. Pg 2195-2207, Nov 20, 2008).

**In summary**, 17,802 men  $\geq$  50yo and women  $\geq$  60yo with no prior history of CV disease, with high-sensitivity CRP (hsCRP)  $\geq$  2.0 mg/l and LDL  $<$  130 mg/d/ were randomized to Crestor 20 mg or placebo. The trial was designed to last 3-4 years (maximum 5 years) but was terminated after a median follow-up of 1.9 years due to overwhelming benefit in the treatment group in the reduction of total cardiovascular events, the primary endpoint. Crestor 20mg/day reduced LDL by 50% and hsCRP by 37% which resulted in significant relative risk reductions of:

- 44% for the primary endpoint (MI, Stroke, Arterial Revascularization, Hospitalization for unstable angina or death from CV causes: 142 pts on Crestor vs. 251 pts on placebo;  $p < 0.00001$ ).
- 65% reduction in non-fatal MI (22 on Crestor vs. 62 placebo;  $p < 0.00001$ )

- 54% reduction in total MI (31 Crestor vs. 68 placebo; p = 0.0002)
- 48% reduction in stroke (33 Crestor vs. 64 placebo; p = 0.002)
- 47% reduction in revascularization and unstable angina (76 Crestor vs. 143 placebo; p < 0.00001)
- 47% reduction in MI, stroke or death from CV causes (83 Crestor vs. 157 placebo; p < 0.00001)
- 20% reduction in death from any cause (198 Crestor vs. 247 placebo; p < 0.02)

The Crestor group did not have a significant increase in myopathy or cancer, but it did have a higher incidence of physician reported diabetes and a slight increase in the median glycated hemoglobin value (5.9% on Crestor vs. 5.8% on placebo). Changes in glucose metabolism with statin therapy is not a new finding: it has been seen with Lipitor, pravastatin and simvastatin. But, once again, the press is overstating this risk. Diabetics were not allowed in this trial, since they require LDLs < 100, but since 90% of diabetics have a CV event and MI's are the leading cause of death in diabetics, and since LDL cholesterol is the leading predictor of a CV event in a diabetic, it is safe to assume that the benefit of lowering LDL by 50% and CV events by almost 50% in this trial would outweigh the risk of increasing the glycated Hgb by one-tenth of a percentage point.

The on-treatment LDLs were <55 in over half of the study participants which was not associated with an increase in myopathy, hepatic injury, cancer or hemorrhagic stroke.

**“In conclusion**, in this randomized trial of apparently healthy men (age ≥ 50) and women (age ≥ 60) who did not have hyperlipidemia but did have elevated levels of hsCRP, the rates of a first major CV event and death from any cause were significantly reduced among the participants who received Crestor 20mg as compared with those who received placebo.” Ridker recommends this simple evidence-based approach to statin therapy for primary prevention.

Among men and women over age 50:

- (1) If diabetic - treat, regardless of baseline LDL.
- (2) If LDL > 160 mg/d - treat.
- (3) If hsCRP > 2 mg/l - treat.

Should you be interested, additional study details including criteria, lab values, outcomes, events and a brief discussion are located on our website at [www.cardassoc.com/jupitertrial](http://www.cardassoc.com/jupitertrial).