

## Drugs in the News 4/6/09 – Analysis of the Rosuvastatin (Crestor) Jupiter Trial

The “Rosuvastatin to Prevent Vascular Events in Men and Women with Elevated C-Reactive Protein” was published in the November 20, 2008 *New England Journal of Medicine*. This trial is also known by the acronym JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin).

The trial was stopped early after a median follow-up of 1.9 years (maximum, 5.0). Rosuvastatin reduced LDL cholesterol levels by 50% and it was concluded “In this trial of apparently healthy persons without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels, rosuvastatin significantly reduced the incidence of major cardiovascular events.”

The trial was financially supported by Astra-Zeneca the maker of rosuvastatin. The *Wall Street Journal* reported that the JUPITER results have been a “boon” to Astra Zeneca with sales of the drug rising 29% last year to \$3.6 billion as rosuvastatin gained ground on other branded cholesterol drugs, including [Pfizer](#) Inc.'s atorvastatin.

The media picked up that there was a 44% relative risk reduction in the rosuvastatin group compared to those receiving placebo. Few in the media reported absolute risk differences between the groups.

### A CLOSER LOOK AT JUPITER

The primary outcome in JUPITER was the occurrence of a first major cardiovascular event, defined as nonfatal myocardial infarction, nonfatal stroke, hospitalization for unstable angina, an arterial revascularization procedure, or confirmed death from cardiovascular causes.

At the time the study was stopped (median followup, 1.9 years; maximal follow-up, 5.0 years), 142 first major cardiovascular events had occurred in the rosuvastatin group, as compared with 251 in the placebo group

### RISK DIFFERENCE FOR THE PRIMARY OUTCOME

The absolute risk difference between the rosuvastatin and placebo groups is calculated at 1.22%. This translates to a Number Needed to Treat (NNT) of about 82 or 82 patients would need to be treated with rosuvastatin for 1.9 years to prevent one primary outcome event.

### RISK OF DEATH FROM ANY DEATH

This is an estimate calculated from the published trial by taking apart the composite endpoint used in JUPITER. The absolute risk difference for death

from any cause was estimated at 0.55% between the groups. This is an NNT of 182.

The New England Journal of Medicine conducted a two question online survey to gauge readers' views of the JUPITER results. The first survey question asked "Do you believe, on the basis of the JUPITER trial results, that the approach to laboratory screening of apparently healthy adults should be changed? Respondents were split 49% answering yes and 51% no.

The second survey question asked "Do you believe, on the basis of the JUPITER trial results, that the therapeutic use of statins in apparently healthy adults should be changed?" Again, the result was split. The response was 48% yes and 52% no.

### SHOULD JUPITER HAVE BEEN STOPPED PREMATURELY?

When there is clear evidence of benefit or harm ethically a trial should be stopped and subjects offered the beneficial treatment or removed from one that is harmful. In the JUPITER trial the absolute risks were so small the trial should have been continued to its planned completion to allow for a full interpretation of the results.

Prematurely, ending a clinical trial on ethical grounds of benefit can be used to market the treatment to those who do not carefully evaluate the published results.

### CONCLUSION

Students and pharmacists investing a small amount of time in "studying a studying" and applying the principles of interpreting clinical research could come up with markedly different views of the therapeutic value of a drug than that reported in the general media.

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