RxFiles Academic Detailing

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Statins in The Media. What are we to make of it?
Crestor Heart Attack Legal Websites, The Latest FDA Statin Warnings and Patients Declining to Take Statins.

Recently a physician sent us a fax regarding concerns over rosuvastatin *Crestor* being raised by U.S. law firms online and various media. The basic premise is that rosuvastatin, used to prevent heart problems, may also cause them in some patients. Faced with patients bringing in such internet clippings, the question arises of how to best respond. Statin safety has been given more visibility with the association of statin use with increased diabetes risk and cognitive impairment as noted by the FDA.[1] **Is there a "quick take" to help physicians and pharmacists address patient concerns regarding outcomes?**

For the topic of statins increasing heart risk, note the following:

- If you are dealing with **secondary prevention** of cardiovascular disease (CVD), there are several high quality randomized controlled trials (RCTs), all noting more benefit than harm with statins on the endpoints of major CV events and all-cause mortality. [Trial durations ≥5 years; e.g. 4S, HPS, LIPID; 10+ year follow-up data with 4S and HPS] [2]

- If you are dealing with **primary prevention of CVD in high risk individuals** (e.g. have multiple risk factors, not just high cholesterol), there are several high quality trials all noting more benefit than harm for statins on the endpoints of major CV events. [Trial durations 3-5 years; e.g. ASCOT, CARDS, WOSCOPS] [2]

- If you are dealing with **primary prevention in lower risk individuals**, then it is not known how the benefit versus harm ratio will play out. This is because statins may be used for long periods of time in individuals with a long life expectancy. In low risk individuals it is possible that other harms such as myopathy, cardiomyopathy/ heart risk, diabetes[3] and cognitive changes[4] could show up and counter the desired benefit. Follow up data for the HPS and 4S trials provide assurance of safety of simvastatin over a period of more than 10 years.

- The best evidence for longer term (≥3-5 years) benefit over harm in moderate risk individuals is with simvastatin and atorvastatin at low-moderate doses. Higher doses are studied in higher risk patients (e.g. post-ACS). Regarding rosuvastatin specifically, the outcome evidence is limited to the JUPITER trial which was stopped early due to benefit after <2years.[5] Although the CV outcomes of the trial were positive, the early termination prevents us from knowing more about long term benefits vs harms. This is especially of interest given the potency of its LDL lowering effect and emerging use in lower risk patients, some of whom could be exposed to the drug for 30+ years.

- If you have a low risk person who has enough muscle or back pain from statins that they quit exercising/walking, then this could also end up doing more harm than good. (See also Q&A: Management of Statin Myopathy[6])

- Trials that provide us with the above evidence have excluded several types of patients (e.g. frail elderly, single risk factor, etc.) and in some cases like the HPS, 10,000 of the 30,000 patients who went through the 4 week run-in period, were deemed not to be good candidates for long-term statin therapy. This leads to the potential that the trial findings apply only to the 2/3 of patients who actually tolerated the initial 4 week trial of the drug.

- Other factors that are emerging include: 1) the impact of genetics/ethnicity and drug interactions on the potential for benefits and harms. 2) A lack of evidence for pursuing LDL targets with unstudied dose or combination regimens.

Bottom line:

- ☐ **If you have a patient with high CV risk, a statin such as atorvastatin ≤ 80mg/day & simvastatin ≤ 40mg/day will have good long-term safety data & very good evidence for consistently doing more good than harm!!! i.e. Benefits far outweigh risks!**
- ☐ **If you have a lower CV risk patient, we really don't know how the long term benefits and harms of long-term statin therapy will play out. Some patients will want therapy; others may want to minimize their exposure to the uncertainties of long-term drug therapy in this phase of life and focus on lifestyle risk reduction strategies.**
- ☐ **For comparative information on statin choice** eg. potency, interactions, trials[2], cost **, see the Lipid Lowering Agents chart at** http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-lipid%20agents.pdf

Loren Regier BSP BA, Brent Jensen BSP , May 02, 2012.

[1] FDA. Statin Drugs-Drug Safety Communication: Class Labeling Change. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm293670.htm
[2] RxFiles: All cause mortality from lipid lowering trials – chart. http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-lipid%20agents-major%20trials.pdf
[3] *Sattar N, Preiss D, Murray HM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials.* Lancet. 2010;375:735-42.
[4] Statins and cognitive function. Pharmacist's Letter/Prescriber's Letter 2008;24(4):240411.
[5] RxFiles Jupiter trial summary. http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Jupiter-trial-overview.pdf
[6] RxFiles Statin Intolerance - Management Considerations: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Statin-Intolerance.pdf