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Rosuvastatin

A Viewpoint by James D. Best

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As a competitive inhibitor of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase, rosuvastatin will become the sixth cholesterol-lowering drug in the statin class. The issues of safety and effectiveness are critical to its role in the treatment of lipid abnormalities, given the wide availability of other drugs in the same class.

Safety is a particularly important consideration, with the recent withdrawal from most countries of cerivastatin because of the risk of severe myositis, particularly when used in conjunction with gemfibrozil. The hepatic selectivity, lack of extensive metabolism in humans, lack of influence of age or sex on pharmacokinetics and low propensity for pharmacokinetic drug interactions all predict a low likelihood of clinically significant drug interactions for rosuvastatin *in vivo*. Safety and efficacy data from ongoing clinical trials is currently being collected to support the use of rosuvastatin in doses of 10 to 40 mg/day in the general population of patients with lipid disorders. Monitoring during widespread clinical use will be necessary to ensure that there are no unforeseen interactions.

On a mg for mg basis, rosuvastatin will now be the most effective single low-density lipoprotein (LDL)-cholesterol lowering agent. Reduction of LDL-cholesterol with rosuvastatin 1mg was 34%, with a further reduction of 4.5% with each doubling of dose, up to a 65% reduction at 80mg. Triglyceride lowering capability of up to 40% appears to track with the LDL-cholesterol response. High-density lipoprotein (HDL)-cholesterol levels rose by 12% with 80 mg/day of rosuvastatin in patients with heterozygous familial hypercholesterolaemia, but results from patients with hypertriglyceridaemia indicate that the maximal rise in HDL-cholesterol is likely to be achieved with doses of 20 mg or more.

Retrospective analyses of secondary prevention trials have demonstrated reduction with statin therapy of inflammatory markers, such as C-reactive protein, that are powerful predictors of cardiovascular risk. It is not known whether this apparent anti-inflammatory effect of statins is independent of LDL-cholesterol lowering, but it will be important to demonstrate that rosuvastatin has similar effects. Similarly, comparison with other agents in clinical endpoint trials will be necessary to confirm the clinical effectiveness of rosuvastatin. ▲