



### **Mixed results with LY518674, novel therapy for lipid disorders**

LY518674, a novel, potent peroxisome proliferator- activated receptor alpha (PPAR-alpha) agonist, showed no advantages compared with fenofibrate, in clinical studies.<sup>1</sup>

In one study, 309 patients with atherogenic dyslipidemia underwent a 4-week placebo run-in period (NCEP ATPIII lifestyle changes and diet) before randomisation to daily treatment with LY518674 10 g, 25 g, 50 g or 100 g, fenofibrate 200 mg or placebo for 12 weeks. Treatment with LY518674 reduced triglycerides by about 35% and raised HDL cholesterol by about 15%; results were similar with fenofibrate. Interestingly, there were smaller increases in HDL cholesterol at the higher doses of LY518674. The increase in LDL cholesterol with LY518674 was 20%, substantially greater than with fenofibrate. Although both treatments were generally well tolerated, serum creatinine was increased 35-38%, suggesting the potential for an adverse effect on kidney function. The study was simultaneously published in the Journal of the American Medical Association.<sup>2</sup>

The second study was conducted in 304 patients with elevated levels of LDL cholesterol. Patients were randomised to treatment with placebo or atorvastatin 10 mg daily during a 4-week run-in period, and then entered a 12-week treatment period, during which they were randomly allocated treatment with placebo, LY518674 10 g or 50 g. In patients previously treated with atorvastatin, adding LY518674 resulted in an incremental decrease of 20-43% in triglycerides, 1-12% increase in HDL cholesterol and a further small reduction in LDL cholesterol. Increases in serum creatinine were observed in about 20% of patients.

### **References**

1. Nissen SE et al. Efficacy and Safety of a Potent New PPAR-Alpha Agonist as Monotherapy or in Combination With Statins in Subjects With Dyslipidemia. Presented at 56<sup>th</sup> Annual American College of Cardiology Scientific Sessions, New Orleans, 24-27 March 2007. Abstract 404-4.
2. Nissen SE, et al. Effects of a potent and selective PPAR- $\alpha$  agonist in patients with atherogenic dyslipidemia or hypercholesterolemia. JAMA 2007; 297:1362-73.