



Further insights on torcetrapib – the ILLUSTRATE trial

Data from ILLUSTRATE, an imaging trial with torcetrapib, show that changes in HDL cholesterol levels are an independent predictor of the beneficial effects of treatment on plaque progression. These data were reported at the Scientific Sessions of the Annual Meeting of the American Heart Association, Orlando November 2007.¹

Background to ILLUSTRATE

The ILLUSTRATE (Investigation of Lipid Level Management Using Coronary Ultrasound to Assess Reduction of Atherosclerosis by CETP Inhibition and HDL Elevation) trial investigated the effect of torcetrapib, in addition to atorvastatin, on atherosclerosis progression in patients with clinical evidence of coronary heart disease (CHD). The study, previously reported in the *New England Journal of Medicine*², failed to show any significant benefit of torcetrapib on the change in % atheroma volume (PAV), as assessed by intravascular ultrasound. This was despite increases in HDL cholesterol of 61% with torcetrapib treatment.

New data

In a new analysis, the ILLUSTRATE investigators reported an inverse relationship between changes in HDL cholesterol and the PAV and total atheroma volume ($p < 0.001$ for each correlation). The greatest increase in HDL cholesterol levels (>80%) was associated with lowest progression of atherosclerosis, as measured by either parameter.

Patients with evidence of regression of atherosclerosis (i.e. a decrease in PAV) had higher HDL cholesterol levels (73 mg/dL vs. 66 mg/dL, $p = 0.02$), as well as greater increases in HDL cholesterol (59.5% vs. 48.3%, $p = 0.02$).

There was no relationship between LDL cholesterol levels and atherosclerosis progression.

These findings suggest that torcetrapib treatment leads to the generation of functional HDL particles, and that other 'off-treatment' effects of torcetrapib may explain its lack of benefit on atherosclerosis progression.

References

1. Nicholls SJ, Brennan DM, Wolski K et al. Changes in levels of high density lipoprotein cholesterol predict the impact of torcetrapib on progression of coronary atherosclerosis: insights from ILLUSTRATE. *Circulation* 2007;116: Abstract 684.
2. Nissen SE et al. Effect of torcetrapib on the progression of coronary atherosclerosis. *N Engl J Med* 2007;356:1304-16.