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LIPIDS

Dalcetrapib raises HDL-cholesterol level, but does not reduce cardiac risk

Dalcetrapib, an inhibitor of cholesteryl ester transfer protein (CETP), raised the HDL-cholesterol level in patients hospitalized with an acute coronary syndrome, but this change failed to translate into a reduction in cardiovascular events. These data from the dal-OUTCOMES trial were presented at the AHA 2012 Scientific Sessions.

In previous studies, a high level of HDL cholesterol has been associated with a reduced risk of cardiovascular disease. To determine whether raising the HDL-cholesterol level by inhibition of CETP reduces cardiovascular risk, the dal-OUTCOMES researchers randomly allocated 15,871 patients with an acute coronary syndrome to receive either 600 mg of dalcetrapib daily or a placebo, in addition to the best-available care (including statins, other drugs, and revascularization).

At the second prespecified interim analysis, 1,135 primary end-point events (death from coronary heart disease, nonfatal myocardial infarction, ischaemic stroke, unstable angina, or cardiac arrest with resuscitation) had occurred. The HDL-cholesterol level had increased by 4–11% in the placebo group, and by 31–40% in patients taking dalcetrapib, from a mean baseline level of 42 mg/dl. Little change occurred in the LDL-cholesterol level. No difference was observed in the rate of the primary end point (8.0% vs 8.3%, respectively; HR 1.04, 95% CI 0.93–1.16, $P = 0.52$) and, thus, the trial was terminated early (median follow-up 31 months).

Other CETP inhibitors—evacetrapib and anacetrapib—are undergoing phase III testing. These drugs might raise HDL-cholesterol and lower LDL-cholesterol levels more than dalcetrapib, and have a beneficial impact on clinical outcomes.

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Original article Schwartz, G. G. *et al*. Effects of dalcetrapib in patients with a recent acute coronary syndrome. *N. Engl. J. Med*. doi:10.1056/NEJMoa1206797