

## Anacetrapib safely lowers LDL and raises HDL

**Key point:** According to results from the DEFINE (Determining the Efficacy and Tolerability of Cholesteryl Ester Transfer Protein [CETP] Inhibition with Anacetrapib) trial, presented as a late-breaking clinical trial at the American Heart Association's Scientific Sessions 2010 and published in the *New England Journal of Medicine*, anacetrapib (Merck) increased HDL cholesterol levels and decreased LDL cholesterol levels in patients with dyslipidemia without serious adverse effects.

**Finer points:** DEFINE was a randomized, double-blind, multicenter trial of 1,623 patients with coronary heart disease (CHD) or CHD risk equivalents given anacetrapib 100 mg or placebo daily for 18 months. Anacetrapib is an investigational reversible CETP inhibitor.

Patients in the DEFINE trial were already receiving at least one dyslipidemia agent, including a statin; had achieved target LDL levels between 50 and 100 mg/dL; and were instructed to follow the Therapeutic Lifestyle Changes or similar cholesterol-lowering diet. All patients had an HDL level less than 60 mg/dL. The mean age of patients was 63 years (range 18–79 years); 77% of patients were men and 68% were white.

After 24 weeks, anacetrapib reduced LDL by 40% (81 mg/dL to 45 mg/dL,  $P < 0.001$ ) and increased HDL by 138% (41 mg/dL to 101 mg/dL,  $P < 0.001$ ) from baseline. After 18 months of anacetrapib use, data indicated no significant changes from baseline in aldosterone, blood pressure, liver function test, or electrolyte (sodium, chloride, potassium, or bicarbonate) levels. Patient reports of muscle symptoms were similar between treatment and placebo groups.

**What you need to know:** Despite the effective use of statin therapy, some patients continue to experience cardiovascular (CV) events. The CETP enzyme transfers cholesterol from HDL to LDL; therefore, inhibition of CETP reduces LDL and increases HDL. Torcetrapib, the first CETP inhibitor studied in Phase III trials, also reduced LDL and increased HDL. In clinical trials, however, torcetrapib use was associated with increased blood pressure, which could potentially increase mortality and CV events; as a result, further study of torcetrapib was discontinued.

The DEFINE trial was not designed to assess the effects of anacetrapib on CV events; however, fewer events occurred in the anacetrapib group than in the statin-only group. Study limitations included inadequate power to provide definitive results regarding the overall safety and efficacy of anacetrapib. Few nonwhite patient populations were evaluated; therefore, future studies should assess efficacy and safety in other races and ethnic groups. The efficacy and safety of anacetrapib will be further evaluated in a larger Phase III trial called REVEAL (Randomized Evaluation of the Effects of Anacetrapib Through Lipid-Modification).

**What your patients need to know:** Educate patients that anacetrapib is one of a new class of drugs that lowers bad (LDL) cholesterol levels and increases good (HDL) cholesterol levels when given with other lipid-lowering drugs like statins. Explain that results from studies are promising, but further study is needed to determine if this new drug helps prevent heart attacks. Encourage patients to exercise regularly and to follow a low-cholesterol diet under the supervision of their prescriber.

**Sources:**

- Cannon CP et al. [Primary results of the DEFINE trial: determining the efficacy and tolerability of CETP inhibition with anacetrapib.](#) *Circulation.* 2010;122:2215–26.
- Cannon CP. [Primary results of the DEFINE trial: determining the efficacy and tolerability of CETP inhibition with anacetrapib.](#) Oral presentation.
- Cannon CP et al. [Safety of anacetrapib in patients with or at high risk for coronary heart disease.](#) *N Engl J Med.* 2010;363:2406–15.

**Related resources on [www.pharmacist.com](http://www.pharmacist.com):**

- ADIL, November 2006. [Torcetrapib increases HDL cholesterol in clinical trial.](#)
- ADIL, December 2006. [Safety concerns: Torcetrapib trials ended.](#)

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