# 新薬はHDLを有意に上昇させLDLをほぼ半分に低下させる（Abstract＃21824）

## DEFINE：CETP阻害剤anacetrapibはLDLおよびHDLコレステロールに多大な効果を有する

## DEFINE: CETP inhibitor anacetrapib has large effect on LDL and HDL cholesterol

ある治験薬はこのクラスの他の薬剤で認められた血圧上昇がなく高密度リポ蛋白(HDL)コレステロールレベルを2倍以上に上昇させ低密度リポ蛋白(LDL)コレステロールを半分近く低下させたとのレイトブレイキング臨床試験結果が2010年AHA学会で発表され同時にNew England Journal of Medicine 2010年11月17日号に掲載された。AnacetrapibによるCETP阻害の効果および忍容性の評価(Determining the EFficacy and Tolerability of CETP INhibition with AnacEtrapib：DEFINE)は20ヵ国153施設において1,623人の患者(平均年齢62.5歳；女性23%；アジア人、黒人または多人種17%、ヒスパニック15%)にコレステロールエステル輸送蛋白(CETP)阻害剤anacetrapib 100mgまたはプラセボを18ヵ月間内服させた無作為化二重盲検試験である。患者は既にスタチンおよび/または他の脂質低下薬で治療されており、LDLコレステロールレベルの目標を達成していた。AnacetrapibはLDLを811mg/dLから49mg/dLへと40%低下させた。またHDLレベルは40mg/dLから101mg/dLに上昇した。参加者の血圧や電解質に変化はなかった。

## Full Text

An experimental drug more than doubles the level of high-density lipoprotein cholesterol (HDL) and cuts low-density lipoprotein (LDL) cholesterol nearly in half without the blood pressure increase linked to another agent in its class, according to late-breaking clinical trial results presented at the American Heart Association's Scientific Sessions 2010.

Determining the EFficacy and Tolerability of CETP INhibition with AnacEtrapib (DEFINE) is a randomized, double-blind trial of 1,623 patients who took either 100 mg of the cholesterylester transfer protein (CETP) inhibitor anacetrapib, or a placebo for 18 months at 153 centers in 20 countries. The patients were already being treated with a statin and/or other lipid-lowering medicine and had achieved their goal level of LDL cholesterol.

The study's primary endpoints were the percent change in LDL and safety as measured by a number of clinical and laboratory measures as well as cardiovascular (CV) events.

Anacetrapib reduced LDL by 40 percent - from 81 mg/dL to 49 mg/dL. It also more than doubled the level of HDL from 40 mg/dL to 101 mg/dL without raising blood pressure.

"Anacetrapib has a knock-your-socks-off effect on HDL and a jaw-dropping effect on LDL," said Christopher P. Cannon, M.D., senior investigator of the TIMI Study Group in the cardiovascular division of Brigham and Women's Hospital in Boston, Mass. "These changes are striking because virtually all the patients in the study were already taking cholesterol-lowering drugs and achieved previously unattainable levels of good and bad cholesterol."

The experimental drug is one of a new class that blocks the ability of the CETP enzyme to transfer cholesterol particles from HDL to LDL.

Elevated LDL and low levels of HDL are both risk factors for cardiovascular disease. Statins reduce LDL and lessen cardiovascular risk. Despite statin therapy, many patients still have a high risk of cardiovascular disease.

High natural levels of HDL are associated with lower cardiovascular risk, which is why researchers have been looking for ways to increase HDL levels, said Cannon, an associate professor of medicine at Harvard Medical School.

"No treatments raise HDL levels as substantially as seen here (more than doubling of the levels)," said Cannon.

Patients in DEFINE were 62.5 years old on average; 23 percent were women; 17 percent were Asian, black or multiracial and 15 percent were Hispanic. The study included interim safety analyses at six and 12 months, and researchers found no change in blood pressure or electrolytes among participants.

Levels of aldosterone, a hormone produced in the adrenal gland that affects kidney function and blood pressure, didn't change. The researchers also found no increase in muscle problems or liver function abnormalities between groups - a side effect occasionally associated with statins.

Although the study was not designed or powered to assess the effects of anacetrapib on cardiovascular events, fewer cardiovascular events occurred in the anacetrapib group than in the statin-only group. The full efficacy and safety of anacetrapib will be evaluated in a larger Phase III trial, Cannon said.

"This agent provides us a very strong add-on treatment to statins that dramatically increases the good cholesterol and dramatically further decreases the bad cholesterol," he said. "If the cardiovascular effects are borne out by future research, it would be a very promising approach to reducing cardiovascular events in patients with or prone to atherosclerosis."

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