

# Mixed results for weight loss drug on slowing progression of coronary disease

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The anti-obesity medication rimonabant showed mixed results in slowing progression of coronary artery disease in patients with abdominal obesity and pre-existing coronary disease, according to a new study in the April 2 issue of JAMA. The study is being released early online April 1 to coincide with its presentation at the annual conference of the American College of Cardiology.

“Abdominal obesity, even in the absence of type 2 diabetes, is associated with a constellation of metabolic and physiological abnormalities that amplify the risk for atherosclerotic cardiovascular disease,” the authors write in background information for the article. Atherosclerotic disease, often commonly known as “hardening” of the arteries, occurs when deposits of plaques accumulate in the inner lining of the arteries. The researchers write that there are few treatment options to address the underlying cause of the metabolic syndrome – abdominal obesity. One promising approach is the use of the selective cannabinoid type 1 receptor antagonist rimonabant. Rimonabant has not been approved by the U.S. Food and Drug Administration, but is available in several other countries. Metabolic syndrome includes high triglyceride levels, a low HDL (good) cholesterol level, high blood pressure, and a high level of glucose (sugar) in the blood.

In this study called STRADIVARIUS, the Strategy to Reduce Atherosclerosis Development Involving Administration of Rimonabant – The Intravascular Ultrasound Study, ultrasonographic coronary imaging was used to assess atherosclerotic progression. Steven E. Nissen, M.D.,

of the Cleveland Clinic and the STRADIVARIUS investigators, conducted a randomized, double-blinded clinical trial from December 2004 to December 2005 comparing rimonabant with placebo in 839 patients at 112 centers in North America, Europe and Australia. The patients were randomly assigned to receive either rimonabant (20 mg daily) or a matching placebo for 18 to 20 months. Patients were eligible to participate in the study only if they also required a coronary angiography for a medical reason. The patients returned for scheduled clinic visits at 3, 6, 12, and 18 months following randomization. The main outcome the researchers were observing was a change in the percent atheroma volume (PAV) and the secondary outcome was a change in normalized total atheroma volume (TAV). PAV and TAV are different measurements of plaque build-up in an artery.

“In the rimonabant vs. placebo groups, PAV increased 0.25 percent vs. 0.51 percent, respectively, and TAV decreased  $-2.2\text{mm}^3$  vs. an increase of  $0.88\text{mm}^3$ ,” the researchers report. “Rimonabant-treated patients had a larger reduction in body weight ( $-4.3\text{kg}$  [ $-9.5\text{ lbs.}$ ] vs.  $-0.5\text{ kg}$  [ $-1.1\text{ lbs.}$ ]) and greater decrease in waist circumference ( $-4.5\text{ cm}$  [ $-1.77\text{ inches}$ ] vs.  $-1.0\text{ cm}$  [ $-0.39\text{ inches}$ ]). In the rimonabant vs. placebo groups, high-density lipoprotein cholesterol levels increased  $5.8\text{mg/dL}$  (22.4 percent) vs.  $1.8\text{mg/dL}$  (6.9 percent) and median (midpoint) triglyceride levels decreased  $-24.8\text{ mg/dL}$  (20.5 percent) vs.  $-8.9\text{ mg/dL}$  (6.2 percent).” However, LDL-C (“bad” cholesterol) levels and blood pressure changes did not differ significantly between treatment groups. “Psychiatric adverse effects were more common in the rimonabant group (43.4 percent vs. 28.4 percent),” the researchers note. Anxiety and depression were the most often reported adverse effects.

“Administration of rimonabant, 20mg, daily for 18 months did not significantly reduce the rate of progression of coronary disease for the primary IVUS (intravascular ultrasound) end point, the change in PAV,” the authors write. “However, the secondary endpoint, change in TAV,

showed a statistically significant treatment effect favoring rimonabant.”

In conclusion, the authors write: “Because the current study failed to achieve a statistically significant effect for the primary efficacy measure, additional studies will be required to further define the role of rimonabant in the treatment of abdominally obese patients with coronary disease and metabolic risk factors.”

Source: JAMA and Archives Journals

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