Rimonabantと冠動脈疾患の進行

STRADIVARIUSトライアルの結果からは、冠動脈疾患を有する肥満患者の動脈プラークの進行をリモナバント療法により遅延できると結論付けることはできない

STRADIVARIUS trial is inconclusive regarding ability of rimonabant therapy to slow progression of arterial plaque in obese patients with coronary disease

新たなスタディデータはリモナバント療法が冠動脈疾患を有する肥満患者の動脈プラークの進行を遅延させることができると証明するには不十分である、とのLate-Breaking Clinical Trialの結果がAmerican College of Cardiology学会で発表された。STRADIVARIUSにおいて839人がrimonabant（1日20mg）またはプラセボを、18～20ヵ月投与する群に無作為に割り付けられた。医学的な理由により冠動脈造影を要する患者のみ組み入れ可とした。対象者らは無作為割付後3、6、12、および18ヵ月後に予定受診をした。主な超音波上の評価項目はアテローム容積のパーセント変化であり、二次評価項目は、プラークの負荷を異なる方法で計測した、標準化総アテローム容積であった。Rimonabant群とプラセボ群とで、パーセントアテローム容積はそれぞれ0.25%および0.51%増加したが、二次評価項目ではrimonabantの方が成績が良好で、それぞれ2.2mm^{3}の減少と0.88mm^{3}の増加であった。

Full Text

New study data are inadequate to prove whether rimonabant therapy can slow progression of arterial plaque in obese patients with coronary disease, according to a late-breaking clinical trial presented at the annual meeting of the American College of Cardiology.

In 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, MD, of the Cleveland Clinic and colleagues 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.

Patients were randomized to rimonabant (20 mg daily) or matching placebo for 18 to 20 months. Patients were eligible to participate in the study only if they also required 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 versus placebo groups, PAV increased 0.25 percent versus 0.51 percent, respectively, and TAV decreased -2.2mm^3 vs. an increase of 0.88mm^3," the researchers reported.

"Rimonabant-treated patients had a larger reduction in body weight (-4.3kg [-9.5 lbs.] vs. -0.5 kg [-1.1 lbs.]) and greater decrease in waist circumference (-4.5 cm [-1.77 inches] vs. -1.0 cm [- 0.39 inches]). In the rimonabant vs. placebo groups, high-density lipoprotein cholesterol levels increased 5.8mg/dL (22.4 percent) vs. 1.8mg/dL (6.9 percent) and median (midpoint) triglyceride levels decreased -24.8 mg/dL (20.5 percent) vs. -8.9 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 said. "However, the secondary endpoint, change in TAV, showed a statistically significant treatment effect favoring rimonabant."

The authors concluded that 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."

ACC2008 特集