

Synopsis of RIO-Lipids Reprint

Publication Information

Title: Effects of Rimonabant on Metabolic Risk Factors in Overweight Patients with Dyslipidemia

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Objective

To study the effects of rimonabant on metabolic risk factors, including adiponectin levels, in high-risk patients who are overweight or obese and have untreated dyslipidemia

Design

- ◆ One-year study period
- ◆ Randomized, double-blind, placebo-controlled, multicenter study
- ◆ Patients randomized to receive placebo, rimonabant 5 mg, or rimonabant 20 mg (1:1:1 ratio, respectively)
- ◆ Single blind, 4-week placebo run-in period with mildly hypocaloric diet (600 kcal/day deficit) that was continued through the study

Patient Population

- ◆ 1,036 adult patients
- ◆ Body mass index (BMI): 27–40
- ◆ Presence of untreated dyslipidemia: triglycerides > 150–700 mg/dL (1.69–7.90 mmol/L), or ratio of cholesterol to high-density lipoprotein cholesterol (HDL-C) of > 4.5 in women and > 5 in men

Endpoints

- ◆ *Primary:* Change in body weight
- ◆ *Secondary:* Changes in levels of HDL-C, triglycerides, glucose, insulin (during an oral glucose tolerance test), metabolic syndrome, waist circumference, leptin, adiponectin, and relevant biochemical cardiovascular markers (for example, C-reactive protein); and assessment of safety

Results

- ◆ *Weight change:* Rimonabant 20 mg induced significant weight loss compared with placebo: -19 lb (-8.6 kg) rimonabant 20 mg vs. -5.1 lb (-2.3 kg) placebo using the repeated-measures (RM) model for completers (which provided a better estimate of the true effect of the drug than last observation carried forward [LOCF]); with the LOCF analysis, weight loss was -15.2 lb (-6.9 kg) rimonabant 20 mg vs. -3.3 lb (-1.5 kg) placebo ($P < 0.001$)

- ◆ *Waist circumference:* Rimonabant 20 mg induced a significant decrease in waist circumference compared with placebo: -9.1 cm with rimonabant 20 mg vs. -3.4 cm with placebo ($P < 0.001$) using RM; and -7.1 cm vs. -2.4 cm using LOCF
- ◆ *Triglycerides:* Levels decreased -15.8% with rimonabant 20 mg vs. -3.6% with placebo ($P < 0.001$) using RM; -12.6 vs. -0.2 using LOCF
- ◆ *HDL-C:* Levels increased 23.4% with rimonabant 20 mg vs. 12.2% with placebo ($P < 0.001$) using RM; 19.1% vs. 11.0% using LOCF
- ◆ *Plasma adiponectin:* Levels of plasma adiponectin increased by 57.7% with rimonabant 20 mg using RM and 46.2% using LOCF ($P < 0.001$), a change that was partly independent of weight loss
- ◆ *Other factors:* Rimonabant 20 mg also showed significant improvement over placebo in changes in low-density lipoprotein particle size, glucose tolerance, fasting and post-challenge insulin levels, C-reactive protein levels, and the proportion of patients with metabolic syndrome
- ◆ *Safety profile:* The rates of completion for the study were similar among those receiving placebo and rimonabant 5 mg and 20 mg. The most frequent adverse events causing discontinuation were depression, anxiety, and nausea

Conclusions

- ◆ CB₁-receptor blockade with rimonabant significantly reduces body weight and waist circumference and improves a number of metabolic risk factors in overweight or obese patients who have atherogenic dyslipidemia
- ◆ The adverse-event profile in this study was similar to that in the RIO-Europe study
- ◆ The weight-loss-independent effect of rimonabant on plasma adiponectin levels is consistent with rimonabant's in vitro effect on adiponectin production by adipocytes