Context Rimonabant, a selective cannabinoid-1 receptor blocker, may reduce body weight and improve cardiometabolic risk factors in patients who are overweight or obese.
Objective To compare the efficacy and safety of rimonabant with placebo each in conjunction with diet and exercise for sustained changes in weight and cardiometabolic risk factors over 2 years.
Design, Setting, and Participants Randomized, double-blind, placebocontrolled trial of 3045 obese (body mass index _30) or overweight (body mass index _27 and treated or untreated hypertension or dyslipidemia) adult patients at 64 US and 8 Canadian clinical research centers from August 2001 to April 2004.
Intervention After a 4-week single-blind placebo plus diet (600 kcal/d deficit) run-in period, patients were randomized to receive placebo, 5 mg/d of rimonabant, or 20 mg/d of rimonabant for 1 year. Rimonabant-treated patients were rerandomized to receive placebo or continued to receive the same rimonabant dose while the placebo group continued to receive placebo during year 2.
Main Outcome Measures Body weight change over year 1 and prevention of weight regain during year 2. Additional efficacy measures included changes in waist circumference, plasma lipid levels, and other cardiometabolic risk factors.
Results At year 1, the completion rate was 309 (51%) patients in the placebo group, 620 (51%) patients in the 5 mg of rimonabant group, and 673 (55%) patients in the 20 mg of rimonabant group. Compared with the placebo group, the 20 mg of rimonabant group produced greater mean (SEM) reductions in weight (−6.3 [0.2] kg vs −1.6 [0.2] kg; *P*_.001), waist circumference (−6.1 [0.2] cm vs −2.5 [0.3] cm; *P*_.001), and level of triglycerides (percentage change, −5.3 [1.2] vs 7.9 [2.0]; *P*_.001) and a greater increase in level of high-density lipoprotein cholesterol (percentage change, 12.6 [0.5] vs 5.4 [0.7]; *P*_.001). Patients who were switched from the 20 mg of rimonabant group to the placebo group during year 2 experienced weight regain while those who continued to receive 20 mg of rimonabant maintained their weight loss and favorable changes in cardiometabolic risk factors. Use of different imputation methods to account for the high rate of dropouts in all 3 groups yielded similar results. Rimonabant was generally well tolerated; the most common drug-related adverse event was nausea (11.2% for the 20 mg of rimonabant group vs 5.8% for the placebo group).
Conclusions In this multicenter trial, treatment with 20 mg/d of rimonabant plus diet for 2 years promoted modest but sustained reductions in weight and waist circumference and favorable changes in cardiometabolic risk factors. However, the trial was limited by a high drop-out rate and longer-term effects of the drug require further study.
Clinical Trials Registration ClinicalTrials.gov Identifier: NCT00029861
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