Rimonabant improves cardiometabolic risk factors in overweight/obese patients with poorly controlled type 2 diabetes (HbA1c ≥8%) on monotherapy with metformin or sulfonylureas

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Background and Aims: Rimonabant, the first selective CB1 receptor blocker, significantly improved HbA1c, fasting glucose, triglycerides, HDL-cholesterol, body weight and waist circumference in a randomised clinical trial in overweight/obese patients with type 2 diabetes treated with metformin (65%) or sulfonylureas (35%) (RIO-Diabetes [N=1047]). Baseline HbA1c was 7.3% in this study. At 1 year, changes in mean HbA1c were j0.1% and j0.6% with rimonabant 5 and 20 mg/day vs +0.1% for placebo (p=0.034 and p<0.001 vs placebo, respectively). In this analysis, the benefits of rimonabant in the subset of patients with poor glycaemic control (HbA1c ≥8%) were assessed.

Material and Methods: We evaluated the efficacy and tolerability of rimonabant therapy in patients with HbA1c <8% (N=833) or ≥8% (N=188) at baseline. All patients received a hypocaloric diet (600 kcal/day deficit) throughout the study in addition to study treatment with either placebo or rimonabant (5 mg/day or 20 mg/day).

Results: Compared with placebo, rimonabant 20 mg/day significantly decreased body weight and waist circumference from baseline to 1 year in both patient subgroups, as well as improving glycaemic and lipid risk factors (Table). In the HbA1c ≥8% group, 30.2% of patients receiving rimonabant 20 mg/day had HbA1c <7% at 1 year compared with 11.1% of those receiving placebo (p=0.012). The corresponding proportions of patients with HbA1c <6.5% were 14.3% and 1.9% (p=0.02). Within the HbA1c <8% and ≥8% groups, respectively, 5.4% and 6.6% of patients receiving placebo discontinued therapy as a result of a treatment-emergent adverse events compared with 15.6% and 13.6% of patients receiving rimonabant 20 mg/day.

Among the adverse events leading to discontinuation with rimonabant 20 mg/day, those already reported in the
previous papers, i.e. psychiatric disorders, nervous system disorders and gastrointestinal disorders, were reported with the following frequency in patients with HbA1c <8% or Q8%, respectively: 6.3% vs 1.5%; 1.9% vs 4.5% and 3.7% vs 0%.

Conclusion: Rimonabant 20 mg/day improved glycaemic control irrespective of patients’ baseline HbA1c levels. In patients with HbA1c Q8% (who were already receiving metformin or a sulfonylurea) reduction from baseline in HbA1c of 1.1% was observed with rimonabant 20 mg/day, along with significant improvements in HDL-cholesterol and triglycerides. Rimonabant 20 mg/day was generally well tolerated. These findings support the use of rimonabant 20 mg/day for improving glycaemic control and reducing cardiometabolic risk in overweight/obese patients with type 2 diabetes.

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