Rimonabant improves cardiometabolic risk factors in overweight/obese patients with poorly controlled type 2 diabetes (HbA1cQ8%) 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 Q8%) were assessed.
Material and Methods: We evaluated the efficacy and tolerability of rimonabant therapy in patients with HbA1c <8% (N=833) or Q8% (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 HbA1cQ8% 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% andQ8% 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 HbA1cQ8% (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.

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 Q8%) were assessed.

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	HbA_{1c} <8%		HbA_{1c} ≥8%	
	Placebo	Rimonabant 20 mg/day	Placebo	Rimonabant 20 mg/day
Mean change from baseline at 1 year in:	(N=279)	(N=269)	(N=61)	(N=66)
Body weight (kg)	−1.4	−5.5***	−1.6	−4.9***
Waist circumference (cm)	−1.9	−5.5***	−2.0	−4.3*
HbA_{1c} (%)	0.2	−0.5***	−0.3	−1.1***
Fasting glucose (mmol/L)	0.5	−0.4***	−0.3	−1.7*
Fasting insulin (µIU/mL)	0.6	−0.5	0.4	−1.3
Triglycerides (%)	8.9	−6.2***	−0.4	−21.3***
HDL-cholesterol (%)	7.2	15.4***	7.1	16.3*

Data are for ITT population, last observation carried forward.

*p<0.05; ***p≤0.001 vs placebo.

Supported by sanofi-aventis