

Rimonabant

A Viewpoint by Eli V. Gelfand

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Obesity and the metabolic syndrome have recently cast a shadow on the steady increase seen in life expectancy in the developed world. Both conditions are associated with a markedly increased risk of developing diabetes mellitus and clinically significant atherosclerosis. Pharmacological treatment of obesity mainly consists of appetite suppressants and stimulants, but none of these therapies significantly improve the associated comorbidities of obesity, such as dyslipidaemia and glucose intolerance. Recently, new insights have been gained into the role of the endogenous cannabinoid system in regulation of human metabolism. It appears that endocannabinoids, through their action on the specific cannabinoid (CB)-1 and CB-2 receptors in the brain and adipose tissue, enhance the central orexigenic drive and increase peripheral lipogenesis.

Rimonabant is the first available CB-1 receptor blocker. Rimonabant was originally synthesised in 1994, and since that time it has been studied in several randomised, controlled clinical trials, focused on patients at risk for cardiovascular disease. Administration of rimonabant to patients with obesi-

ty and at least one other cardiac risk factor (hypertension or dyslipidaemia) results in a significantly greater weight loss than placebo. In addition, the proportion of patients meeting formal criteria for metabolic syndrome decreases significantly over the course of treatment with rimonabant. Favourable effects on the lipid profile are typically observed, with a decrease in serum triglycerides and an increase in high-density lipoproteins. In obese patients with type 2 diabetes, therapy with rimonabant improves glucose control, with clinically significant decreases in glycosylated haemoglobin levels. Data from the RIO-NA trial suggest that continuing treatment with rimonabant beyond 1 year is necessary to maintain the achieved weight loss.

The unique nature of rimonabant lies in its effect on several components of the metabolic cascade. Indeed, its dual action in the brain and adipose tissue is, in part, responsible for its beneficial effects on weight loss, waist circumference, glucose utilisation and lipid profile. Of course, therapy with rimonabant is unlikely to be used as the sole method of weight loss. Rather, rimonabant could be part of a comprehensive programme of pharmacotherapy, hypocaloric diet, regular physical exercise and perhaps stress reduction to achieve a significant, sustainable weight loss. ▲