

an excellent tolerance among patients, except for some mild gastrointestinal adverse effects at the highest dose administered. Some adverse effects on mental function have been noticed in some patients, and that is why this drug should not be prescribed to patients with a medical history of depression or pronounced mental symptoms. Safety data from the preliminary results of the RIO-Lipids, RIO-Europe, RIO-North America and STRATUS-US trials revealed that Rimonabant is well tolerated among patients^{13,14,15}. The most frequently reported adverse effects are nausea, dizziness and upper respiratory infections. Diarrhea was seen most commonly in the RIO-Europe trial (2.3%, 5.8% and 7% for placebo, Rimonabant 5 mg/day and 20 mg/day, respectively).

ADVANTAGES

Rimonabant is reported to increase HDL-C and decrease atherogenic LDL-C levels. The unique property of this drug may, in turn, improve cardiovascular risk factors and metabolic syndrome.

In addition to weight loss, rimonabant is reported to produce improvement in HbA1C levels and may be helpful in diabetes.

It also prevents weight gain in persons who are quitting smoking.

Evidence: Clinical studies in obese subjects have documented weight loss, improved glucose metabolism, and lipid control, as well as reduced blood pressure in patients with type 2 diabetes^{16, 17, 18}. Other effects seen in some but not all studies include increased rates of smoking cessation. It is important that Rimonabant is currently being evaluated for effects on cardiovascular morbidity and mortality end points versus placebo in a randomized controlled study, the Comprehensive Rimonabant Evaluation Study of Cardiovascular End Points and Outcomes (CRESCENDO) study, with expected results in 2011¹⁹. This trial is recruiting patients with inclusion criteria: waist circumference >102 cm (40 inches) in males, >88 cm (35 inches) in females, with one coronary heart disease equivalent or two major risk factors for CVD.

CONCLUSION

Rimonabant, the selective blocker of CB1 receptors, may normalize the activity of the endocannabinoid system, resulting in weight loss, reduced waist circumference, improvement in lipid and glucose metabolism in obese people and may prevent weight gain associated with smoking cessation along with medical nutritional therapy and increased physical activity. The positive effects may, in turn, improve cardiovascular and metabolic risk factors. Future research and the

results of ongoing clinical trials of this exciting drug are required to establish its long-term therapeutic implications and safety profile.

REFERENCES

1. Lindström J, Louheranta A, Mannelin M, Rastas M, Salminen V, Eriksson J, Uusitupa M, Tuomilehto J, Finnish Diabetes Prevention Study Group: The Finnish Diabetes Prevention Study (DPS): lifestyle intervention and 3-year results on diet and physical activity. *Diabetes Care* 2003;26: 3230–3236.
2. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM: Diabetes Prevention Program Research Group: Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002 346:393–403.
3. Lindström J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemio K, Hannalainen H, Harkonen P, Keinanen-Kiukkaanniemi S, Laakso M, Louheranta A, Mannelin M, Paturi M, Sundvall J, Valle TT, Uusitupa M, Tuomilehto J, Finnish Diabetes Prevention Study Group: Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet* 2006 368:1673–1679.
4. Holt R: Orlistat reduces features of the metabolic syndrome: the XENDOS study. *Diabetes Obes Metab* 2003; 5:356.
5. Torgerson JS, Hauptman J, Boldrin MN, Sjörström L: XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155–161.
6. Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M: STOP-NIDDM Trial Research Group: Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. *Lancet* 2002; 359:2072–2077.
7. DREAM (Diabetes REduction Assessment with ramipril and rosiglitazone Medication) Trial Investigators, Gerstein HC, Yusuf S, Bosch J, Pogue J, Sheridan P, Dinccag N, Hanefeld M, Hoogwerf B, Laakso M, Mohan V, Shaw J, Zinman B, Holman RR: Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. *Lancet* 2006 ; 368:1096–1105.
8. Iversen L. Cannabis and the brain. *Brain* 2003;126:1252–70.
9. Rinaldi-Carmona M, Barth F, Heaulme M. Biochemical and pharmacological characterization of SR141716A, the first potent and selective brain cannabinoid receptor antagonist. *Life Sci* 1995;56:1941–7.
10. Compton DR, Aceto MD, Lowe J, Martin BR. In vivo characterization of a specific cannabinoid receptor antagonist (SR141716): inhibition of delta-9-tetrahydrocannabinol induced responses and apparent agonist activity. *J Pharmacol Exp Ther* 1996;277:586–94.
11. Cota D, Marsicano G, Tschöp M. The endogenous cannabinoid system affects energy balance via central orexigenic drive and peripheral lipogenesis. *J Clin Invest* 2003;112:423–31.
12. Coizet V, Cassel JC, Kelche C. Effects of the selective CB1 cannabinoid receptor antagonist, SR141716, on cognitive performance in intact, brain-damaged and scopolamine-treated rats. *Behav Pharmacol* 1998;9:25.
13. Van Gaal L. RIO-Europe: A randomized, double-blind study of weight reducing effect and safety of rimonabant in obese patients with or without comorbidity. Program and abstracts from the European Society of Cardiology Congress 2004, Aug 28-Sep1; Munich, Germany; 2004.
14. Press release. [accessed 2004 Nov 9]. Available from: http://en.sanofi-aventis.com/press/p_press_2004.
15. Results from the RIO-North America trial show that first year improvements in cardiovascular risk factors are maintained in the second year of treatment. American Society of Cardiology Congress, 2004 Nov 9 (online).
16. Van Gaal LF, Rissanen AM, Scheen AJ, Ziegler O, Rossner S, RIO-Europe Study Group: Effects of the cannabinoid-1 receptor blocker rimonabant on weight reduction and cardiovascular risk factors in overweight patients: 1-year experience from the RIO-Europe study. *Lancet* 2005; 365:1389–1397.
17. Despres JP, Golay A, Sjörström L: Rimonabant in Obesity-Lipids Study Group: Effects of rimonabant on metabolic risk factors in overweight patients with dyslipidemia. *N Engl J Med* 2005; 353:2121–2134.
18. Pi-Sunyer FX, Aronne LJ, Heshmati HM, Devin J, Rosenstock J, RIO-North America Study Group: Effect of rimonabant, a cannabinoid-1 receptor blocker, on weight and cardiometabolic risk factors in overweight or obese patients: RIO-North America: a randomized controlled trial. *JAMA* 2006; 295:761–775.
19. CRESCENDO Comprehensive Rimonabant Evaluation Study of Cardiovascular Endpoints and Outcomes. *ClinicalTrials.gov Identifier: NCT00263042 (sanofi-aventis)*.

NOBLE PRIZE IN MEDICINE

Three European scientists who discovered virus that causes cervical cancer and AIDS share this year's Noble prize in Medicine. A German virologist, **Harald zur Hausen**, will receive half the award for discovery of HPV, the human papilloma virus, according to the announcement made on Monday by the Karolinska Institute in Stockholm. The discovery led to the development of a vaccine against cervical cancer, the second most common cancer in women. The institute said the other half of the award will be shared equally by two French virologists, **Francoise Barre-Sinoussi** and **Luc Montagnier**, for their discovery of virus of AIDS. Since its discovery in 1981, AIDS has rivaled the worst epidemics in the history.

An estimated 25 million more are living with HIV. Dr. Zur Hausen of the University of Heidelberg was cited for discovering the first HPV, Type 16, in 1983 from biopsies of woman who had cervical cancer. A year later, Dr. Zur Hausen cloned HPV 16 and another type, 18. The two HPV types are consistently found in about 70% of cervical cancer biopsies throughout the world, the institute said. Of the more than 100 human papilloma viruses now known, about 40 infect the genital tract, and 15 of them put women at the high risk for cervical cancer. Papilloma viruses account for more than 5% of all cancers worldwide. Discovery of HIV led to Blood tests to detect the infection and the infection and to anti-retroviral drugs that are effective in prolonging the lives of the patients. The discovery has also led to an understanding of the natural history of HIV infection, which ultimately lead to AIDS unless treated. "Never before has the science and medicine been so quick to discover, identify the origin and provide treatment for a viral infections," the Karolinska Institute said.