I’ve heard that a new weight-loss drug is coming out on the market. What is it and how does it work?

Answer provided by Anthony Vu Huynh, DO

Waiting in the Wings: Rimonabant for Weight Reduction

Rimonabant was developed by the pharmaceutical company Sanofi-Aventis. It had some positive effects on weight-loss, cardiovascular risk factors and helping people quit smoking. In February 2006, the FDA did not approve rimonabant as a smoking cessation medication, but announced possible approval as a weight-loss drug with undisclosed requirements. While rimonabant is waiting for possible FDA approval in the United States, it has been available in the United Kingdom since June 2006, and in Germany since September 2006 for weight-loss management.

How does rimonabant work?

Rimonabant acts on the endocannabinoid system (ECS). Cannabinoid substances, found in marijuana and isolated in 1964, have some effect on appetite stimulation. In the early 1990s, studies traced the receptors binding these substances in animals, then found anandamide, the first cannabinoid substance. In 1995, the second cannabinoid substance was discovered in gut and brain, named 2-AG. Hence, the ECS exists in animals unrelated to the use of marijuana. Subsequently, the ECS was determined to play a role in regulation of energy balance, food intake and metabolic processes.

The relationship between ECS and appetite control has been demonstrated in several studies in rats. In one study done in the United Kingdom in 1999, the rats were fed with 30 grams of food, and then half of them received injections of cannabinoid substance. The result was over-eating behavior observed in these rats compared to the ones that did not receive cannabinoid substance. The second study in 2002 was also in the United Kingdom, where they measured the levels of these cannabinoid substances in rats before and after eating. They found the level increased before meal and decreased after meal, mainly in the brain. These findings confirmed the effect of cannabinoid substances in appetite control.

Rimonabant works by blocking the receptor of the cannabinoid substances in the brain as well as the gastrointestinal tract, fat tissues, heart and liver. As the result, it suppresses appetite, as well as produces changes in body fat and glucose metabolism.

How do we know rimonabant works in humans?

“RIO-North America” was a large study conducted at multiple centers across North America from August 2001 to April 2004 with 3,045 overweight and obese adult participants. In this study, after four weeks of a low-calorie diet and increased activity
levels, patients were given either a placebo (no active ingredient) or two different doses of rimonabant (5mg/day or 20mg/day) for one year. The average weight-loss after one year was 6.3 kg in the 20 mg dose group versus 1.6 kg in the placebo group, and the waist circumferences was reduced in the two groups, 6.1 cm versus 2.5 cm, respectively. There was no significant weight-loss seen in the lower dose (5mg/day) group.

After the first year of the study, the patients on rimonabant were randomly reassigned to either receive placebo or continue the same dose of 5mg and 20mg; while the original placebo group continued receiving the placebo. At the end of the two-year period, the group who continued the 20mg dose of rimonabant was able to maintain an average weight-loss from baseline of 7.4 kg (16 pounds), whereas the treated patients who switched to a placebo regained most of their weight. There was no significant weight-loss during the second year in the groups taking the placebo or the low dose rimonabant (5mg/day) for two years. The results showed that the weight-loss in patients taking 20mg of rimonabant is clinically significant and well maintained during the second year.

Regarding rimonabant’s effect on cardiovascular risk factors, the study showed increased levels of high density lipoprotein cholesterol (HDL-C, or “good” cholesterol) and decreased levels of fasting insulin in patients receiving either 5mg or 20mg of rimonabant, but the triglycerides levels decreased only in patients receiving the 20mg dose. Levels of total cholesterol and LDL-C (“bad” cholesterol) were not significantly different among the three studied groups. In addition, a subgroup study showed that more smokers on 20mg rimonabant quit smoking than smokers on placebo (27.6 percent versus 16.1 percent).

**Is rimonabant safe?**

In terms of the safety of rimonabant, the percentage of patients who dropped out of the study due to adverse reactions were 7.2 percent in placebo group, 9.4 percent in the 5mg dose group and 12.8 percent in the 20mg dose group. Those side effects observed were mild and short term including psychiatric disorders (depressed mood, anxiety, irritability, and insomnia), nervous system effects (headache, dizziness) and gastrointestinal tract problems (nausea, diarrhea). There was no increase in heart rate, change in electrocardiogram or other cardiovascular problems.

In conclusion, the two-year data from the phase III multicenter RIO trials showed positive result for weight-loss and cardiovascular risk factors after one year of treatment with rimonabant and was sustained over the two-year period with tolerable side effects. The cost for one month supply of 20mg per day of rimonabant is about 80 euros or 102 U.S. dollars. Sanofi-Aventis optimistically thinks that this drug will be available in the U.S. by the end of this year. The major question is whether insurance companies will see the benefit, not only for weight-loss but also for a reduction in cardiometabolic risk factors.

**About the Author:**

Anthony Vu Huynh, DO, is doing a Bariatrics and Nutrition Fellowship at Geisinger Medical Center in Danville, PA after finishing his Internal Medicine training at Caritas Saint Elizabeth Medical Center, Boston, MA. He is an alumni of NSU-COM, Fort Lauderdale, Fla.

**References**

1. Antheneli, RM: Effects of rimonabant in the reduction of major cardiovascular risk factors. Results from the STRATUS-US trial.
The mission of the Obesity Action Coalition is to elevate and empower those affected by obesity through education, advocacy and support.

About the OAC

The Obesity Action Coalition is a non-profit patient organization dedicated to educating and advocating on behalf of the millions of Americans affected by obesity. By strictly representing the interests and concerns of obese patients, the OAC is a unique organization with a patient-focused approach to obesity. To learn more about the OAC, visit www.obesityaction.org or contact the National Office at (800) 717-3117.

OAC Resources

Through education and advocacy, patients need to get involved to help drive change in the obesity community. The OAC provides several beneficial resources for patients, as well as professionals.

- OAC Introductory Brochure
- Obesity Action Alert
- OAC News
- State-specific Advocacy Guides
- Understanding Obesity Brochure
- Understanding Obesity Poster
- Advocacy Primer: Your Voice Makes a Difference
- The OAC Web site: www.obesityaction.org

All OAC resources are complimentary and may be ordered in bulk. To request materials or an order form, please contact the OAC National Office at (800) 717-3117 or send an email to info@obesityaction.org.

OAC membership

Membership in the Obesity Action Coalition allows the patient voice to be heard in the fight against obesity. By building a coalition of members, consisting of patients, family members and professionals, the OAC strives to educate and advocate on behalf of the millions who are affected by obesity. Membership benefits include:

- Official charter membership card/certificate
- OAC News - the OAC's quarterly newsletter
- Subscription to Obesity Action Alert - a monthly e-newsletter
- Representation through advocacy, in addition to information on advocacy issues concerning patients

Membership Application

Name: ________________________________
Company Name: _______________________
Address: ______________________________
City: __________ State: _____ Zip: _________
Phone: ________________________________
E-mail: ________________________________

Payment Information

Enclosed is my check made payable to the Obesity Action Coalition for $_____.

Please charge my credit card for my membership fee of $_____

Credit Card #: ________________________
Expiration: ______ Name on Card: ________
Signature: ____________________________

* Different benefits apply. Contact the OAC National Office for more info.

Please mail to: Obesity Action Coalition
4511 North Himes Ave, Suite 250
Tampa, FL 33614
Or fax to: (813) 873-7838

If you have questions about OAC membership, please contact the National Office at (800) 717-3117.