Greatest Weight Loss Effect With Combination Therapy

	Placebo	Naltrexone 48 mg	Bupropion 200 mg	Bupropion 200 mg and Naltrexone 32 mg
Weight loss	**–1%**	**–2%**	**–3%**	**–7%**
Body fat loss	–4%	–3%	–4%	–12%
Visceral fat loss	–5%	–0%	–2%	–14%
Waist circumference	–1 cm	–3.8 cm	–2.9 cm	–5.4 cm
Fasting glucose	+1.9 mg/dL	+3.4 mg/dL	+3.5 mg/dL	–2.0 mg/dL
Insulin	+0.9 U/mL	+1.7 U/mL	–0.5 U/mL	–3.0 U/mL
Triglycerides	–15 mg/dL	–17.6 mg/dL	–18.4 mg/dL	–43.6 mg/dL

Note: Based on a randomized study of 419 nondiabetic obese subjects treated for 24 weeks.
Source: Dr. Greenway

Drug Combo Yields Better Weight Loss

BY FRAN LOWRY
Orlando Bureau

ELSEVIER GLOBAL MEDICAL NEWS

NEW ORLEANS — Combination therapy with bupropion and naltrexone resulted in superior weight loss, compared with placebo or either drug alone, Dr. Frank L. Greenway said at the annual meeting of NAASO, the Obesity Society.

Patients randomized to the experimental bupropion-naltrexone combination achieved a 1.5- to twofold greater weight loss after 24 weeks of treatment than did those randomized to monotherapy with bupropion or naltrexone, or to placebo.

The combination patients also achieved a greater improvement in insulin resistance and markers of cardiovascular disease risk, such as waist circumference and triglyceride levels, said Dr. Greenway, chief of the outpatient clinic at Louisiana State University's Pennington Biomedical Research Center, Baton Rouge.

The multicenter trial randomized 419 healthy, nondiabetic obese subjects to receive 200 mg bupropion twice a day; 48 mg naltrexone once a day; 200 mg bupropion combined with 16, 32, or 48 mg naltrexone twice a day; or placebo. The patients also received an exercise prescription and were placed on a diet.

A subset of 75 randomized subjects had a DEXA scan to measure body fat, and 73 randomized subjects had a multislice abdominal CT scan to measure visceral fat. The measures were taken at baseline and at 24 weeks, as were insulin, glucose, and triglyceride analyses. Patients treated with the bupropion-naltrexone combination showed a statistically significant greater total body weight loss, compared with placebo or monotherapy subjects. Orexigen Therapeutics Inc., San Diego, provided the combination drug.

The greatest weight loss effect was observed for the combination that included naltrexone at the dose of 32 mg, he said. Subjects randomized to that regimen lost a mean of 7% of their body weight, 12% of their body fat, and 14% of their visceral fat. Waist circumference also was reduced by a mean of 5.4 cm.

In addition, their insulin levels declined by a mean of 3 mcU/mL, fasting glucose fell by a mean of 2 mg/dL, and triglyceride levels fell by a mean of 44 mg/dL, all of which were statistically significantly greater than the values for the other regimens.

The naltrexone-bupropion combination promotes hypothalamic proopiomelanocortin activity, which reduces appetite and stimulates energy expenditure, thereby preventing an early plateau or slowing down of weight loss.

Bupropion and naltrexone have been approved by the Food and Drug Administration for treating addictive disorders, but the combined formulation has not been approved. "We expect the new [combination] drug application to be submitted in 2009," said Dr. Greenway, who disclosed that he is a consultant for Orexigen Therapeutics. ■