Two New Weight Loss Drugs Show Potential

BY HEIDI SPLETE

WASHINGTON — Two novel weight loss drugs led to significant losses in overweight and obese adults, according to the findings from two phase III, placebo-controlled trials that were presented at the annual meeting of the Obesity Society.

The drugs are not yet approved by the Food and Drug Administration.

In one study, Dr. Caroline Apovian of Boston University Medical Center presented results of the Contrave Obesity Research II (COR-II) study, a phase III, double-blind trial of 1,496 adults with an average age of 44 years and an average body mass index of 36 kg/m^2. The study involved Orexigen Therapeutics Inc.'s combination naltrexone SR/bupropion SR combination therapy (Contrave).

Participants were randomized to a single daily oral dose of the combination drug NB32 (32 mg naltrexone/360 mg bupropion) or a placebo.

After 28 weeks, 56% of the treatment group participants achieved at least a 5% weight loss—the study's primary outcome measure—compared with 18% of the placebo group. A 10% weight loss was achieved by 27% of the treatment group and 7% of the placebo group; 15% loss was achieved by 10% and 2% of the groups, respectively. Baseline demographics were similar between the treatment and placebo groups.

After 28 weeks, participants were rerandomized to a combination drug including 48 mg naltrexone and 360 mg bupropion (NB48). "This was a chance to see if there was a higher dose needed," she said, but at 56 weeks, there was no significant change in weight loss with NB48 compared with NB32.

The patients in the treatment group reported significant decreases in food cravings compared with baseline, Dr. Apovian said.

Approximately half of the patients in the drug and placebo groups discontinued the study, but discontinuation rates due to adverse events were low. Nausea, which was the most common adverse event, was mild or moderate in most cases, "and occurred mostly in the first 4 weeks," she said.

The combination drug seemed to be well tolerated and the safety profile was consistent with previous data on the two drugs when used separately, she added. Dr. Apovian serves on the advisory board of Orexigen and has received financial support from other pharmaceutical companies, including Lilly and Amgen. Orexigen intends to submit the drug for FDA approval in the first half of 2010, according to a company statement.

Dr. Lee Kaplan of Harvard University, Boston, presented results of a study of lorcaserin, a selective 5HT2C agonist designed to promote weight loss without the cardiovascular side effects associated with nonspecific 5HT agonists.

The randomized, double-blind, placebo-controlled phase III study enrolled 4,008 patients, aged 18-65 years, for 52 weeks. The study involved patients with a BMI of 27-45 kg/m^2 with and without at least one comorbid condition. The average age was 44 years, average BMI was 36 kg/m^2, and 80% were female. Baseline demographics were similar between the treatment and placebo groups.

Overall, the intent-to-treat analysis showed that a 5% weight loss was achieved by 47% of participants who took 10 mg lorcaserin twice daily, by 40% of those who took 10 mg lorcaserin once daily, and by 25% of those who took a placebo, said Dr. Kaplan, who is also director of the Massachusetts General Hospital weight center.

Patients in the twice-daily, once-daily, and placebo groups who completed the study according to the protocol lost an average of 7.7 kg, 6.5 kg, and 3.9 kg, respectively. The most common adverse events were headache, fatigue, dizziness, and nausea, each of which occurred in less than 5% of patients.

Patients with FDA-defined valvulopathy were included in the study, and the lorcaserin was not associated with increased valvulopathy during the study, Dr. Kaplan added.

Dr. Kaplan has received financial support from lorcaserin's manufacturer, Arena Pharmaceuticals, among other pharmaceutical companies. ■