Novel Weight-Loss Combo May Lower BP

BY DAN HURLEY

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF HYPERTENSION

NEW YORK — An investigational weight-loss agent that combines two drugs slightly reduced blood pressure in an analysis of three large placebo-controlled clinical trials involving a total of 3,985 patients.

The once-daily drug combines a low dose of the generic stimulant phentermine with a low-dose, controlled-release version of the antiepileptic topiramate. The two drugs have been shown previously to cause weight loss by different mechanisms, Dr. Suzanne Oparil said at the meeting.

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DR. BAKRIS

Higher doses of phentermine are occasionally associated with increased blood pressure, but the combined product appeared to produce enough weight loss—more than 10% of body weight after 56 weeks in two of the studies—to result in modestly lower blood pressure, reported Dr. Oparil, director of the vascular biology and hypertension program at the University of Alabama at Birmingham.

"We really need a well-tolerated, safe, and effective weight-loss treatment," commented Dr. Oparil, a past president of ASH who conducted the analysis as a consultant to Vivus, which is developing the combined agent under the brand name Qnexa.

But some physicians at the ASH meeting said they were not entirely convinced of the agent's safety. At the highest dose, a heart rate increase of about 1.5 beats per minute was observed. And none of the trials used 24-hour ambulatory blood pressure monitoring.

"I would want to see data on the drug's effect on 24-hour blood pressure," said Dr. George L. Bakris, professor of medicine and director of the Hypertension Center at the University of Chicago.

The 56-week EQUIP trial enrolled 1,267 obese adults and compared the high-dose combination (phentermine 15 mg and topiramate 92 mg) and a low-dose combination (phentermine 3.75 mg and topiramate 23 mg) with placebo. The 28-week EQUATE trial (enrolled 756 obese adults and compared the high-dose formulation and a mid-dose formulation (phentermine 7.5 mg and topiramate 46 mg) with placebo and with the respective single agents. The 56-week CONQUER trial enrolled 2,487 overweight and obese adults with two or more weight-related comorbidities: increased waist circumference, type 2 diabetes, elevated triglycerides, and elevated blood pressure. It compared the high-dose and mid-dose combinations with placebo. Of the total 4,510 patients who were initially enrolled in the three trials, 3,985 completed the studies.

In Dr. Oparil's pooled analysis of the three trials, the mean weight loss at week 28 was 1.9% of total body weight for the

VITALS

Major Finding: In patients on the highest dose of phentermine plus controlled-release topiramate, systolic blood pressure reductions were significantly lower than with placebo: 3.4 mm Hg after 28 weeks in EQUATE, 3.8 mm Hg after 56 weeks in EQUIP, and 3.2 mm Hg after 56 weeks in CONQUER.

Data Source: Pooled analysis of data on 3,985 patients in three clinical trials.

Disclosures: Dr. Oparil disclosed relationships with Vivus as well as with Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi Sankyo, Forest, Gilead, Merck, NicOx, Novartis, the Salt Institute, Sanofi-Aventis, and Takeda. Dr. Bakris has reported financial relationships with Abbott, Gilead, GlaxoSmithKline, Merck, Novartis, and other companies.

1,579 patients on placebo, 5.1% for the 234 patients on the lowest dose of the drug, 8.0% for the 591 patients on the middle dose, and 9.9% for the 1,581 patients on the highest dose. All three active-treatment groups had significantly more weight loss, compared with the placebo group.

In the two trials that went to 56 weeks, CONQUER and EQUIP, weight loss reached 10.4% of body weight with the highest dose, compared with 1.5% with placebo, also a significant difference.

The reductions in systolic blood pressure in patients on the high-dose combination, compared with placebo, were 3.4 mm Hg after 28 weeks in EQUATE, 3.8 mm Hg after 56 weeks in EQUIP, and 3.2 mm Hg after 56 weeks in CONQUER; all three reductions were statistically significant. Significant reductions in systolic blood pressure also were seen with some of the lower doses of the combined product. For diastolic blood pressure, only two of the higher-dose groups had reductions that were significantly greater than that seen with placebo.

"In the hypertensive subgroup [of CONQUER], there were significant and dose-related reductions in both systolic and diastolic blood pressure," Dr. Oparil said. In that subgroup, the mean drop in systolic blood pressure was 6.9 mm Hg for the 256 patients given the middle dose of the drug and 9.1 mm Hg for the 514 patients given the highest dose of the drug; both reductions were significantly greater than the 4.9–mm Hg reduction in the 516 patients on placebo. Reductions in diastolic blood pressure in these patients were 5.2 mm Hg for the middle dose and 5.8 mm Hg for the highest dose; both reductions were significantly greater than the 3.9–mm Hg drop with placebo. ■

Chances for Exercise Are Few for Some

BY ROBERT FINN

Only 20% of census blocks nationwide have parks within a half-mile of their boundary, according to a report issued by the Centers for Disease Control and Prevention. Furthermore, 50% of U.S. youths say they lack access to parks, community centers, and sidewalks in their neighborhoods.

The State Indicator Report on Physical Activity, 2010 also documented that only 17% of high school students report getting the recommended 1 hour of exercise per day. Only 65% of adults reported being physically active, which the report defined as 150 minutes per week of moderate physical exercise, 75 minutes per week of vigorous physical exercise, or a combination of the two.

In a prepared statement, First Lady Michelle Obama tied the lack of physical activity to this lack of access. "Today's report shows that too many kids are spending too much time in front of the computer or TV or a video game or have limited access to physical activity, because they live in neighborhoods that aren't safe, go to schools where PE classes have been cut, or live in communities where there are no sports leagues or after-school activity programs," she said. "We need parents and teachers, business and community leaders, and the public and private sectors to come together to create more opportunities for kids to be active so they can lead happy, healthy lives."

VITALS

Major Finding: Fifty percent of American youths have no parks, community centers, and sidewalks in their neighborhoods. Only 17% of high school students are physically active.

Data Source: Data from a variety of behavioral surveys administered between 2006 and 2009.

Disclosures: None was reported.

In preparing the report, the CDC compiled data from a variety of behavioral surveys administered between 2006 and 2009.

Other findings from the report include:

► Nationwide, only 30% of high school students take daily physical education classes.

► A total of 25% of adults say they engage in no leisure-time physical activity whatsoever.

► Only 20 states require or recommend that elementary schools provide scheduled recess.

► Fewer than half (46%) of middle schools and high schools support walking or biking to and from school. ■

The full report is available at http://www.cdc.gov/physicalactivity/downloads/PA_State_Indicator_Report_2009.pdf.