

# 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 previ-

ously to cause weight loss by different mechanisms, Dr. Suzanne Oparil said at the meeting.

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.



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DR. BAKRIS

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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 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

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.

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**For patients with type 2 diabetes  
whose blood glucose is not controlled  
with OADs alone**

**IT MAY BE TIME  
TO CONSIDER  
A LANE  
CHANGE**

## 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 combi-

nation, 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 class-

**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.

es 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."

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](http://www.cdc.gov/physicalactivity/downloads/PA_State_Indicator_Report_2009.pdf).

## ADVERTISEMENT

### AS DIABETES PROGRESSES, OADs ALONE MAY NOT BE ENOUGH

According to the UKPDS, up to 50% of  $\beta$ -cell function may be lost by the time patients are diagnosed with type 2 diabetes, and it may continue to decline, on average, by about 5% annually.<sup>1</sup> A recent article by DeFronzo showed that, in patients with highly impaired glucose tolerance, as much as 80% of  $\beta$ -cell function may be lost by the time of diagnosis.<sup>2</sup> It is this progressive  $\beta$ -cell function loss that is primarily responsible for the development of diabetes and the incremental rise in A1C.<sup>2</sup>

Patients may not know that their pancreas is no longer making enough insulin and that their disease has progressed.<sup>3,4</sup> National data from 2003 to 2004 showed that about 40% of patients with diabetes did not have adequate glycemic control.<sup>5a</sup> And because blood glucose control is important, all available therapeutic options—including insulin—should be considered in the treatment of diabetes. Helping patients get their blood glucose under control may help reduce their risk of developing long-term complications.<sup>6</sup>

Many patients with type 2 diabetes may eventually need insulin to achieve or maintain glycemic control.<sup>3,7</sup> Unfortunately, by the time patients with type 2 diabetes are typically prescribed insulin, they may have had diabetes for 10 to 15 years and may already have complications due to a prolonged period of uncontrolled blood glucose.<sup>8</sup>

Patients may blame themselves for what they perceive as 'failure' to control their glucose levels.<sup>3</sup> And because patients' attitudes toward their disease play an important role in diabetes self-care behaviors, it's likely that this negative mindset may adversely impact diabetes self-management.<sup>9</sup>

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Learn more at [www.RethinkInsulin.com](http://www.RethinkInsulin.com)

**References:** 1. Holman RR. *Diabetes Res Clin Pract.* 1998;40(suppl):S21-S25. 2. DeFronzo. *Diabetes.* 2009;58(4):773-795. 3. Polonsky WH, Jackson RA. *Clin Diabetes.* 2004;22(3):147-150. 4. American Diabetes Association. *Clin Diabetes.* 2007;25(1):39-40. 5. Hoerger TJ, Segel JE, Gregg EW, Saaddine JB. *Diabetes Care.* 2008;31(1):81-86. 6. Stratton IM, Adler AI, Neil HAW, et al. *BMJ.* 2000;321(7258):405-412. 7. Hirsch IB, Bergenstal RM, Parkin CG, Wright E, Buse JB. *Clin Diabetes.* 2005;23(2):78-86. 8. Nathan DM. *N Engl J Med.* 2002;347(17):1342-1349. 9. Egede LE, Ellis C. *Diabetes Technol Ther.* 2008;10(3):213-219. 10. Data on file, sanofi-aventis U.S. LLC. 11. Brunton SA, Davis SN, Renda SM. *Clin Cornerstone.* 2006;8(suppl 2):S19-S26. 12. Nathan DM, Buse JB, Davidson MB, et al. *Diabetes Care.* 2009;32(1):193-203. 13. AACE/ACE Consensus Statement. *Endocr Pract.* 2009;15(6):540-559.

### A POSITIVE "INSULIN TALK" MAY HELP REASSURE PATIENTS

The results of having a positive insulin talk can be impactful: in a survey, about 80% of patients with type 2 diabetes who were taking oral antidiabetic drugs (OADs) said they'd consider taking insulin if their doctor recommended it.<sup>10</sup>

By starting the dialogue now, you can help your patients have a better understanding of insulin and the glucose-lowering role it plays as part of an overall diabetes treatment plan, which may include diet, exercise, and other diabetes medications.<sup>3,11</sup>

For appropriate patients, starting insulin earlier in the disease continuum can help improve glycemic control.<sup>7,11-13</sup> The American Diabetes Association states that insulin is the most effective agent for lowering blood glucose.<sup>12</sup>

So, engage patients in talks early and as needed to help turn their negative mindset of failure into a positive opportunity to manage their blood glucose.

Insulin is indicated to help improve glycemic control in patients with diabetes mellitus.

Treatment plans and glycemic targets should be individualized for each patient.

### IMPORTANT SAFETY INFORMATION ABOUT INSULIN

Possible side effects may include blood glucose levels that are too low, injection site reactions, and allergic reactions, including itching and rash. Other medications and supplements could change the way insulin works. Glucose monitoring is recommended for all patients with diabetes.

<sup>a</sup> Defined as A1C <7%. UKPDS=United Kingdom Prospective Diabetes Study.

**INSULIN**  
IMPROVING BLOOD GLUCOSE CONTROL SHOULDN'T WAIT

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