

# With Liraglutide, More Patients Achieve 'Zindex'

BY SHERRY BOSCHERT

SAN FRANCISCO — The once-daily drug liraglutide may work better than other diabetes medications to help patients reach a combination of goals, a secondary analysis of data from pivotal liraglutide studies suggests.

The Food and Drug Administration approved use of liraglutide (Victoza) in January for adults with type 2 diabetes who fail first-line drug therapy, based on data from the pivotal Liraglutide Effect and Action in Diabetes (LEAD) studies. Liraglutide is an injectable human glucagonlike peptide-1 (GLP-1) analogue.

The LEAD trials were "truly heroic" in their number, breadth, and head-to-head comparisons with existing diabetes medications, and in most of those trials liraglutide was more effective at lowering hemoglobin A<sub>1c</sub> levels, Dr. John B. Buse said at a meeting sponsored by the American Diabetes Association.

He reported on an analysis that combined data from the more than 3,900 patients in the LEAD studies to compare the effectiveness of various therapies at achieving a composite end point known among diabetologists as a "Zindex" (because the idea was first proposed by Dr. Bernard Zinman, professor of medicine at the University of Toronto).

The analysis assessed the proportion of patients achieving the Zindex of an HbA<sub>1c</sub> level below 7% with no weight gain and no confirmed hypoglycemia (minor or severe) by the end of the 26- to 52-week studies. A significantly greater proportion of patients on 1.8 mg/day of liraglutide achieved this Zindex (39%),

compared with those on twice-daily injections of the GLP-1 agonist exenatide (24%) or patients treated with glargine (15%), a sulfonylurea (8%), placebo (8%), or a thiazolidinedione (6%).

"An A<sub>1c</sub> less than 7% without weight gain or hypoglycemia is something that's of substantial interest to patients and clinicians," said Dr. Buse, chief of endocrinology and director of the diabetes care center at the University of North Carolina at Chapel Hill.

A second analysis compared the data with a second Zindex that combines three goals identified as standards of care by the American Diabetes Association in 2008: an HbA<sub>1c</sub> less than 7%, no weight gain, and a systolic blood pressure less than 130 mm Hg. The GLP-1 therapies in general have modest effects on blood pressure and lipids, with potentially greater changes in blood pressure on long-acting GLP-1 agonists, Dr. Buse noted.

Again, a significantly greater proportion of patients on 1.8 mg/day of liraglutide (25%) achieved the second Zindex, compared with patients on exenatide (14%), a sulfonylurea (7%), glargine or placebo (5% each), or a thiazolidinedione (3%). "This is of considerable interest, particularly in our pay-for-performance kind of world," he said. ■

**Disclosures:** Dr. Buse has been a consultant for, or received research support from, Novo Nordisk (which markets liraglutide), and Amylin Pharmaceuticals and Eli Lilly (which together are marketing the long-acting version of Amylin's exenatide). He has held stock in Insulet, which makes an insulin pump.

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# Cardiovascular Risk Factors Still Suboptimal in Diabetes

BY BRUCE JANCIN

SNOWMASS, COLO. — Optimal control of cardiovascular risk factors in diabetic patients in the community setting remains an elusive goal, according to the most recent data from the Framingham Heart Study.

Individuals with diabetes have a two- to threefold greater rate of cardiovascular disease than do those without the disease.

Aggressive control of their cardiovascular risk factors is essential to overcome this markedly increased risk. But the Framingham experience demonstrates that it is not happening, Dr. Patrick O'Gara observed at a conference sponsored by the American College of Cardiology.

A bright spot is the low prevalence of cigarette smoking, down to just under 13% during 2000-2005 in 60-year-olds with diabetes in Framingham. That's even lower than the 17% smoking rate among comparable-age individuals without diabetes.

This rejection of smoking by the Framingham diabetic population over the last 3 decades has been particularly impressive: The prevalence among 60-year-olds with diabetes has steadily fallen from nearly 42% during 1970-1979, to 27.5% in 1980-1989, 18% in 1990-1999, and down to 12.8% in the first half of the last decade, noted Dr. O'Gara of Brigham and Women's Hospital, Boston.

Hypertension is another story altogether. The prevalence of hypertension among 60-year-olds with diabetes in 2000-2005 was 87%, more than twice that of nondiabetic individuals.

Moreover, the prevalence of hypertension among the diabetic population was essentially unchanged since 1970.

The rate of controlled hypertension was less than 27% in 60-year-old diabetic men and women in Framingham during 2000-2005, compared with 45.5% in those without diabetes (Circulation 2009;120:212-20).

Only 40% of diabetic individuals with high LDL cholesterol had it controlled to guideline target levels in 2000-2005.

That's better than the 32% rate among those without diabetes, and a huge improvement over the 13.5% rate in diabetic 60-year-olds during 1990-1999, but a far cry from what is required to erase the high excess cardiovascular risk among the diabetic population, Dr. O'Gara noted.

The prevalence of obesity among diabetic 60-year-olds in 2000-2005 was more than 67%, up sharply from 46% during the prior decade.

The rise in obesity among nondiabetic 60-year-olds was considerably less dramatic, from a 26% prevalence in 1990-1999 to 33% in the most recent data.

"I think we all understand the magnitude of the problem and that some of the solutions to this problem are larger than what we can do on an individual basis, but I encourage us all to keep our eyes on the prize," Dr. O'Gara concluded. ■

**Disclosures:** The Framingham Heart Study is funded by the National Heart, Lung, and Blood Institute. Dr. O'Gara reported having no relevant financial interests.

**The rate of controlled hypertension was less than 27% in 60-year-old diabetic men and women in Framingham during 2000-2005 vs. 45.5% in those without diabetes.**

# Diabetes Risk Awareness, Reduction Efforts Still Lacking

BY SHARON WORCESTER

Although nearly a third of U.S. adults were at high risk for developing type 2 diabetes in 2005-2006, about 7% knew of their risk status, and only about half of those said they adopted risk reduction behaviors, data from the 2005-2006 National Health and Nutrition Examination Survey suggest.

Furthermore, of those who were aware of their risk status and who received health care in the year prior to the survey, only 35% said they were advised by their physician to try to control or lose weight, 37% said they

were advised to reduce fat or calorie intake, and 39% said they were advised to increase physical activity, Linda S. Geiss of the Centers for Disease Control and Prevention, Atlanta, and her colleagues reported.

The data—from 1,391 adults aged 20 years and older without diabetes who participated in the survey—showed that reports of physician advice was strongly associated with reports of engaging in risk-reduction behaviors during the past year. Of those who received physician advice about weight loss or control, diet, and physical activity, 75%, 82%, and 71%, respectively, reported following the ad-

vice, the investigators said (Am. J. Prev. Med. 2010 April [doi: 10.1016/j.amepre.2009.12.029]).

The multivariate adjusted prevalence of trying to control or lose weight, reduce fat or calorie intake, and increase physical activity for those who received advice vs. those who did not was 71.0 vs. 44.2, 81.2 vs. 42.3, and 67.9 vs. 38.4 for each behavior, respectively, the researchers found.

The findings are important because prevention trials consistently show that diabetes risk can be reduced substantially through modest weight loss and increased physical activity. However, improved efforts on the

part of physicians to advise patients about lifestyle modifications are likely to be insufficient, as it has not been shown to be associated with maintaining the changes, they explained.

"Prevention promotion by physicians and other health professionals may be more effective if part of a larger process within healthcare systems and communities to promote behavior change," they wrote. They went on to say that prospective studies of interventions and policies to promote and maintain healthy lifestyles with more objective measures of behaviors and outcomes are needed, as are studies on why and when people are

screened for diabetes and counseled about behavior modification, and studies on what types of counseling are effective.

"Reversing the national trends in diabetes incidence is likely to require multiple tiers of interventions," they wrote, noting a need for increased promotion of risk reduction behaviors, increased availability of evidence-based programs for those at risk, and more efficient identification and awareness of risk on the part of patients, providers, health care systems, and health payers. ■

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