Weekly Exenatide Improves Multiple CV Risks

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NEW ORLEANS — Exenatide, in a novel once-weekly formulation, resulted in simultaneous improvements in blood pressure, lipid levels, and body weight as well as glycemic control in a year-long study in 241 type 2 diabetic subjects.

These multiple metabolic improvements were of clinically meaningful magnitude. Thus, the investigational once-weekly exenatide at 2 mg may be a good option for simultaneous improvement of the multiple cardiovascular risk factors typically present in patients with type 2 diabetes, Dr. Richard Bergenstal said at the annual scientific sessions of the American Heart Association.

At baseline, none of the study participants met the American Diabetes Association–recommended combined goal of a glycosylated hemoglobin below 7%, an LDL cholesterol level of less than 100 mg/dL, and blood pressure below 130/80 mm Hg. After 1 year on exenatide, 36% of participants succeeded in reaching all three targets, according to Dr. Bergenstal, executive director of the International Diabetes Center at the Park Nicollet Institute, Minneapolis.

Exenatide once weekly was well tolerated, with a safety profile like that seen in earlier studies of the twice-daily version of the medication.

Blood pressure in the overall study population dropped by a mean of 6.2 mm Hg systolic and 2.8 mm Hg diastolic from a baseline of 128/78 mm Hg. The observed reductions were even greater in the 65 patients with a baseline systolic blood pressure of 130 mm Hg or more: They experienced a mean decrease of 11.4 mm Hg in systolic and 3.6 mm Hg diastolic blood pressure.

At baseline, 55% of subjects had a systolic blood pressure below 130 mm Hg; this figure climbed to 71% after a year on exenatide. Of 87 patients on antihypertensive medications at baseline, 70 maintained their dosage throughout the year-long study and 9 patients decreased their dosage.

The observed improvement in blood pressure was caused by a mechanism other than weight loss, according to Dr. Bergenstal. Although significant weight loss did occur with long-acting exenatide therapy—a mean reduction of 4.1 kg from a baseline 103 kg—the degree of blood pressure reduction was unrelated to the extent of weight loss.

Dr. Bergenstal noted other metabolic improvements in the open-label study. Triglycerides dropped by a mean of 40.1 mg/dL from a baseline 197 mg/dL; total cholesterol, which was 170 mg/dL at enrollment, fell by 7.9 mg/dL; LDL cholesterol dropped by a nonsignificant 2.2 mg/dL, from a baseline of 89 mg/dL; and glycosylated hemoglobin fell by 2.0%, from a baseline 8.3%.

Exenatide once weekly was well tolerated, with a safety profile like that seen in earlier studies of the twice-daily version of exenatide known as Byetta, approved in 2005 for use as an adjunctive therapy for patients with type 2 diabetes who have not achieved adequate blood glucose control on metformin and/or a sulfonylurea. The chief side effect was mild nausea, which occurred in 29% of patients during the course of a year on therapy. No major hypoglycemic episodes occurred.

The year-long open-label study was an extension of the Diabetes Therapy Utilization: Researching Changes in A_{1c}, Weight and Other Factors Through Intervention With Exenatide Once Weekly (DURATION-1), a published 30-week randomized trial of exenatide once weekly vs. twice daily that demonstrated superior glycemic control with the long-acting drug (Lancet 2008;372:1240-50).

Dr. Bergenstal has served as a consultant to Amylin Pharmaceuticals and Eli Lilly & Co., which funded the study. Amylin has indicated it hopes to file for marketing approval of the once-weekly drug in the first half of 2009. ■