'Real-World' Exenatide Efficacy Falls Short in Study

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — The real-world efficacy of exenatide to lower hemoglobin A_{1c} levels in patients with type 2 diabetes may not always match the success seen in clinical trials, a small retrospective study suggests.

Only 12 (40%) of 30 patients with type 2 diabetes who added the incretin mimetic exenatide to ongoing treatment with oral medications or insulin were still taking exenatide 2 years later. For the group as a whole, much of the weight lost after 6 months of exenatide therapy was regained by 2 years, so final weights were not significantly different from baseline weights, the intent-to-treat analysis found.

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Hemoglobin A_{1c} (HbA_{1c}) levels did not change significantly for the group as a whole, study investigator Dr. Jennifer A. Loh of Georgetown University, Washington, reported at the annual scientific sessions of the American Diabetes Association.

A separate comparison found trends toward decreased HbA_{1c} levels in the 15 patients who were taking oral medications plus exenatide, and increased HbA_{1c} levels in the 15 patients using the off-label combination of insulin and exenatide.

Significant decreases in weight were achieved and sustained only in six patients who took exenatide for 2 years and also were on oral medications, not insulin.

"Real-world efficacy is not sustained in all patients; however, there is a small proportion of these patients who did have sustained efficacy in our group," she said. Further research would be helpful to identify the patients most likely to benefit from exenatide therapy, added Dr. Loh. She and coinvestigator Dr. Stephen C. Clement, also of the university, reported no potential conflicts of interest.

Phase III clinical trials have reported significant, long-term efficacy in lowering HbA_{1c} levels and reducing weight in patients with type 2 diabetes. Weight declined by 2.8 kg on average, and HbA_{1c} levels fell by 0.8% in a 30-week randomized, double-blind controlled trial (Diabetes Care 2005;28:1092-100). In three open-label extension studies lasting 82-156 weeks, HbA_{1c} levels decreased by 1.1%-1.3%, and average weight decreased by 4.7-5.3 kg, she noted.

Those open-label studies did not use intent-to-treat analyses, however, and did not include off-label use of insulin. Clinical practices in the studies may not reflect real-world practices, Dr. Loh said.

In the current study, the investigators retrospectively reviewed data on 47 adults who were treated by a single physician and who started exenatide in 2005, shortly after approval of the drug. In all, 17 patients had incomplete data, including 1 patient who simply refused to be weighed. "This is the real world," Dr. Loh noted.

Of the 30 patients with complete data, 18 (60%) stopped taking exenatide by 2 years. A total of 12 patients stopped because of treatment "failure" and 6 stopped because of side effects.

Patients were moderately obese, with an average body mass index of 35 kg/m^2. Weight loss on exenatide was significant at 6 and 12 months, but by 2 years weights averaged only 2.09 kg less than at baseline, a loss that was not statistically significantly.

HbA_{1c} levels did not change significantly, and averaged 7.7% after 2 years.

The researchers conducted a subanalysis of the 12 patients who stayed on exenatide for 2 years. They found a significant (1.07%) decrease in HbA_{1c} levels, and a significant 4.9-kg loss in weight compared with baseline in the six patients who were taking exenatide and oral medications, but no significant changes were seen in the six patients on exenatide and insulin. The efficacy seen with exenatide and oral medications in those who continued exenatide therapy mirrored results from clinical trials, she noted.

"This is such a small study," cautioned one of the moderators of the session, Dr. Steven Edelman, director of the diabetes care clinic at the Veterans Affairs San Diego Healthcare System. Previous studies did not include insulin, which makes them difficult to compare, he added. ■