# Weekly Exenatide Similar to Daily Liraglutide

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FROM THE ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

LISBON – Reasonably similar glucose-lowering effects and modest weight loss can be achieved in patients with type 2 diabetes who are treated with a once-weekly, extended-release formulation of exenatide or once-daily liraglutide, the DURATION-6 study results show.

Liraglutide resulted in a mean change in hemoglobin $A_{1c}$ of –1.48%, compared with baseline. This was slightly (but not significantly) lower than the result for exenatide, which produced a mean drop in $HbA_{1c}$ of –1.28%. Change in $HbA_{1c}$ was with 2 mg once-weekly exenatide, or 1.8 mg once-daily liraglutide. The mean age of participants was 57 years and the mean duration of diabetes was 8-9 years.

Dr. Buse noted that "modest weight loss" could be achieved with both agents, although results reached statistical significance with liraglutide. The mean change in weight from baseline to post-treatment assessment was –2.68 kg for exenatide and –3.58 kg for liraglutide, with a mean difference of 0.9 kg overall.

However, liraglutide was associated with more gastrointestinal side effects than was exenatide, which may be an influencing factor when clinicians and patients decide which of the glucagonlike peptide–1 (GLP-1) receptor agonist regimens to use.

When liraglutide and exenatide were compared, the incidence of GI adverse events was 20.4% vs. 9.4% for nausea, 13.1% vs. 6.1% for diarrhea, and 10.7% vs. 3.7% for vomiting.

Patients taking liraglutide were more likely than those taking exenatide to discontinue treatment as a result of non-GI treatment-emergent adverse effects (5.3% vs. 2.6%).

No major hypoglycemic episodes were reported during the trial, and Dr. Buse reported no significant difference in minor hypoglycemia between the groups

**VITALS**

**Major Finding:** The mean change in $HbA_{1c}$ from baseline to week 26 was slightly but not significantly lower, when liraglutide- vs. exenatide-treated patients were compared (–1.48% vs. –1.28%, respectively).

**Data Source:** DURATION-6, a multicenter, randomized, parallel-group, open-label trial of 911 patients with type 2 diabetes who were treated with weekly extended-release exenatide (2 mg) or daily liraglutide (1.8 mg) injections for 26 weeks.

**Disclosures:** The study was funded by Amylin and Lilly. Dr. Buse disclosed acting as a consultant or investigator for multiple pharmaceutical companies via his contract with the University of North Carolina at Chapel Hill. Dr. Diamant has acted as a consultant, speaker, or both, for Eli Lilly, Merck, Novo Nordisk, and Sanofi-Aventis. She has also received research support from Amylin, Lilly, Merck, Novartis, Novo Nordisk, and Takeda, and was an investigator of the DURATION-3 trial.

the trial's primary end point, but once-weekly exenatide did not demonstrate noninferiority to once-daily liraglutide.

In addition, significantly more patients who took liraglutide rather than exenatide achieved an $HbA_{1c}$ lower than 7% (60% and 52% of patients, respectively).

These results, from the first head-to-head study comparing the two injected regimens, were discussed in full at the meeting, although they had been previously mentioned in a brief press release from Eli Lilly, which manufactures the once-weekly exenatide formulation (Bydureon) in collaboration with Amylin Pharmaceuticals and Alkermes.

"Both exenatide once-weekly and liraglutide once-daily provided effective glucose control with substantial lowering of $HbA_{1c}$," commented study investigator Dr. John Buse of the University of North Carolina at Chapel Hill, as he presented these data.

DURATION-6 was a 26-week, multicenter, open-label, trial in which 911 patients with suboptimal control of type 2 diabetes were randomized to treatment

(10.8% of patients treated with liraglutide vs. 8.9% for exenatide). Hypoglycemia was more likely if patients were also receiving sulfonylurea therapy.

Bydureon has been approved for use in Europe since June, and is available in the United Kingdom. In the United States, however, the Food and Drug Administration bounced the application back to Amylin and Alkermes last October because of concerns of potential QT prolongation with high circulating levels of the drug. The two companies have since submitted new tQT studies, the results of DURATION-5 (comparing Bydureon with Byetta), and updated safety data from previous studies. The agency is expected to respond in January 2012.

In an interview, Dr. Michaela Diamant, who chaired the session in which the DURATION-6 results were revealed, commented that although there appear to be subtle differences between the regimens studied, the findings could still help clinical decision making, particularly if they are considered alongside the other DURATION trial findings.

**'Modest weight loss' was achieved with both agents, but liraglutide patients had more GI side effects.**

DR. BUSE

"If you have two or three studies, then you can say, 'As a physician, I've seen this evidence and, well, I'm going to discuss [this] with my patients,' " said Dr. Diamant, professor of diabetology and director of the diabetes center at the Free University Medical Center in Amsterdam.

Some patients may prefer the once-daily injections with liraglutide, she suggested, as they then can "see a more direct coupling" with what they are eating and their treatment, whereas others may prefer the less-frequent dosing regimen offered by once-weekly exenatide.

Dr. Diamant noted that even marginally different treatments in terms of efficacy and safety could help tailor diabetes therapy more specifically to the individual. "It's like with insulin," she said. "We have different insulins for [different] patients." ■