

Weekly Exenatide Similar to Daily Liraglutide

BY SARA FREEMAN

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

Easy to teach¹

—Can be used in 6 straightforward steps

Easy to use¹

—Only long-acting insulin pen in which dose can be set from 1 to 80 units in 1-unit steps, dialed both up and down
—Once opened, Lantus[®] SoloSTAR[®] can be used for up to 28 days and is not refrigerated

Easy to inject¹

—Dose cannot be dialed past the number of units left in the pen
—It is important to keep the injection button pressed all the way in and to **slowly count to 10 before withdrawing the needle from the skin**. After a full injection, the number in the dose window will return to zero. These steps help ensure that the full dose has been delivered

Indications and Usage for Lantus[®]

Lantus[®] is a long-acting insulin analog indicated to improve glycemic control in adults and children (6 years and older) with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. Lantus[®] should be administered once a day at the same time every day.

Important Limitations of Use: Lantus[®] is not recommended for the treatment of diabetic ketoacidosis. Use intravenous short-acting insulin instead.

Important Safety Information for Lantus[®]

Contraindications

Lantus[®] is contraindicated in patients hypersensitive to insulin glargine or one of its excipients.

Warnings and Precautions

Monitor blood glucose in all patients treated with insulin. Insulin regimens should be modified cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, or method of administration may result in the need for a change in insulin dose or an adjustment in concomitant oral antidiabetic treatment.

Do not dilute or mix Lantus[®] with any other insulin or solution. If mixed or diluted, the solution may become cloudy, and the onset of action/time to peak effect may be altered in an unpredictable manner. Do not administer Lantus[®] via an insulin pump or intravenously because severe hypoglycemia can occur. Insulin devices and needles must not be shared between patients.

Hypoglycemia is the most common adverse reaction of insulin therapy, including Lantus[®], and may be life-threatening.

Severe life-threatening, generalized allergy, including anaphylaxis, can occur.

A reduction in the Lantus[®] dose may be required in patients with renal or hepatic impairment.

Drug Interactions

Certain drugs may affect glucose metabolism, requiring insulin dose adjustment and close monitoring of blood glucose. The signs of hypoglycemia may be reduced in patients taking anti-adrenergic drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine).

Adverse Reactions

Other adverse reactions commonly associated with Lantus[®] are injection site reaction, lipodystrophy, pruritus, and rash.

Important Safety Information for Lantus[®] SoloSTAR[®]

Lantus[®] SoloSTAR[®] is a disposable prefilled insulin pen. To help ensure an accurate dose each time, patients should follow all steps in the Instruction Leaflet accompanying the pen; otherwise they may not get the correct amount of insulin, which may affect their blood glucose.

Please see brief summary of full prescribing information for Lantus[®] on the following pages.

References: 1. Data on file, sanofi-aventis U.S. LLC. 2. Lantus Prescribing Information. April 2010.

(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

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." ■

For patients with diabetes using an insulin vial and syringe

Take aim with the Lantus® SoloSTAR® pen^a

50% more insulin per prescription^b of Lantus® SoloSTAR® for the same co-pay as a vial and syringe on most insurance plans

Prefilled with Lantus®, the only 24-hour insulin approved exclusively for use once a day to help patients with diabetes aim toward glycemic control²

Scan the QR code with your mobile phone for more information about Lantus® and Lantus® SoloSTAR®.

Here's how to get started:

1. Visit 2dscan.com or search for "ScanLife" in your app store or text "SCAN" to 43588
2. Follow the prompts to download the free application
3. Using the application, take a photo of the QR code through the ScanLife application



Once-Daily
24-HOUR

LANTUS® SoloSTAR®
insulin glargine [rDNA origin] injection

STARring the #1-prescribed insulin^c

^aThe SoloSTAR® pen is recommended for use with Becton, Dickinson and Company pen needles.

^bDepending on how prescription is written.

^cBased on TRx data from IMS Health, NPA™ Monthly database, time period from May 2003 to June 2010.

sanofi aventis

Because health matters

© 2011 sanofi-aventis U.S. LLC

US.GLA.11.02.020