and 52 were significantly greater in the group treated with IDegLira than in those treated with IDeg or liraglutide ($P < .0001$, all).

The decrease in FGP was similar in the IDegLira and IDeg groups (–3.6 mmol/L) and significantly lower when compared with the liraglutide group (–1.75 mmol/L) at 26 weeks ($P < .001$). These decreases were maintained at 52 weeks, when FPG was 5.7, 6.0, and 7.3 mmol/L, respectively. At both 26 and 52 weeks, confirmed hypoglycemia was lowest with liraglutide and highest with IDeg, although rates were low overall. There was a slight increase in weight with IDeg, a decrease with liraglutide, and a slight but significant decrease with IDegLira when compared with either treatment ($P < .001$).

The rates of nausea in patients receiving IDeg and IDegLira were generally lower than they were for liraglutide. Other adverse events were similar across groups, and those for patients taking IDegLira were as expected for the individual components.

In conclusion, the DUAL I study showed that IDegLira was associated with significantly greater reductions in HbA_{1c}, significantly lower risk of hypoglycemia, and no weight gain as compared with IDeg at 52 weeks. When compared with liraglutide, IDegLira had greater reductions in HbA_{1c} and FPG while resulting in fewer GI adverse events. These data provide further support for the long-term safety and sustainability of the glucose-lowering effect of IDegLira.

Once Weekly Exenatide Is Safe and Effective for Long-term T2DM Treatment

Written by Lynne Lederman

Patients with type 2 diabetes mellitus (T2DM) require long-term treatment with a hypoglycemic agent, but these agents can be difficult in terms of patient adherence. Eric J. Klein, MD, Capital Clinical Research Center, Olympia, Washington, USA, presented 6-year follow-up data on the efficacy of a once-weekly formulation of exenatide. The phase 3 Effects of Exenatide Long-Acting Release on Glucose Control and Safety in Subjects With Type 2 Diabetes Mellitus [DURATION-1; NCT00308139] is the longest assessment of a glucagon-like peptide–1 receptor agonist reported to date [MacConell L et al. *Diabetes Metab Syndr Obes.* 2013].

Inclusion criteria for DURATION-1 included T2DM (treated with either diet and exercise or oral antidiabetic agents), HbA_{1c} 7.1% to 11.0%, fasting plasma glucose (FPG) < 16 mmol/L, and body mass index 25 to 45 kg/m^2 [Taylor L et al. *BMC Endocr.* 2011; Buse JB et al. *Diabetes Care.* 2010; Drucker DJ et al. *Lancet.* 2008]. Patients were randomly assigned 1:1 to weekly or twice-daily exenatide. At the end of 30 weeks, patients could continue on the extension trial with weekly exenatide. According to Dr Klein, there were no differences in the baseline characteristics between the intention-to-treat (ITT) population and the 6-year completer population.

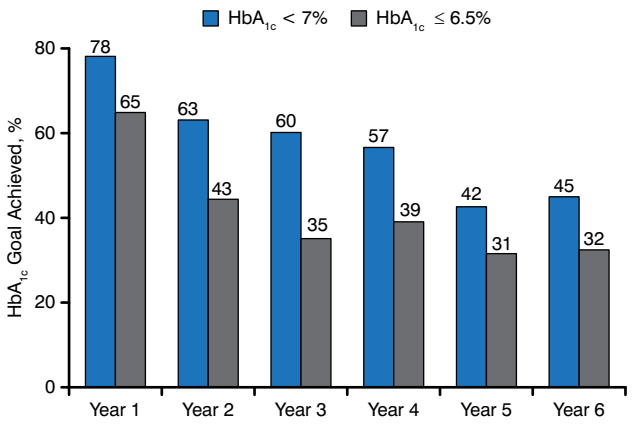
Efficacy data were reported for the population that completed 6 years of follow-up (n = 127). Safety data reported for the ITT population (n = 295) included all individuals who received ≥ 1 dose of exenatide. Drug discontinuation over 6 years of follow-up occurred in 59% of the ITT population (n = 175).

At year 1, the HbA_{1c} level had dropped by 2.2%. The HbA_{1c} level increased over the next 5 years, but at the end of the study the least squares (LS) mean change was –1.6%. The HbA_{1c} level over the entire 6 years was significantly lower than baseline ($P < .05$). The percentages of patients whose HbA_{1c} levels were < 7% or ≤ 6.5% during the course of the study are shown in Figure 1.

FGP decreased by 2.7 mmol/L in the first year. Over the next 5 years, FPG increased but remained lower at study end (–1.6 mmol/L). FPG over the entire 6 years was significantly lower than at baseline ($P < .05$). With regard to weight, patients lost 4.7 kg the first year, regained some weight over the next 2 years, and lost weight again in years 4, 5, and 6. At year 6, the LS mean weight loss was 4.3 kg. Differences from baseline were significantly lower at each year of follow-up except for year 4. There was a decrease in blood pressure after the first year of treatment, but this difference was not sustained over the course of the study.

There were no incremental safety findings, including

Figure 1. Patients Whose HbA_{1c} Levels Were < 7% or ≤ 6.5% Over Time



Six-year completer population (n = 127).

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Table 1. AEs of Special Interest

AE	Incidence and Outcome
Pancreatitis	1 withdrawal, 1 recovered and continued
Pancreatic carcinoma	1 withdrawal
Acute renal failure	4 patients
MACE (serious MI or stroke AEs)	9 patients (3.1%)
MACE (serious MI, unstable angina, stroke, transient ischemic attack, or heart failure AEs)	13 patients (4.4%)

AE, adverse event; MACE, major adverse coronary event; MI, myocardial infarction.

occurrences of major hypoglycemia, observed with long-term treatment. The most common adverse events (AEs) reported included upper respiratory tract infection (43%), nasopharyngitis (29%), diarrhea (27%), sinusitis (24%), and arthralgia (21%). Nausea (mostly mild) and injection-site reactions were the most common AEs with exenatide once weekly during the first 30 weeks, but these were not the most common AEs in the 6 years of follow-up.

Treatment-emergent AEs leading to withdrawal from week 30 to 6 years were infrequent (6.6%); 107 serious AEs were reported in 61 patients from week 30 to year 6. AEs of special interest are listed in Table 1.

In conclusion, long-term therapy with once-weekly exenatide is feasible and well tolerated. This treatment regimen resulted in sustained improvements in glycemic control and weight over 6 years in the 40% of enrollees who continued therapy.

GLUCO-CABG: No Reduction in Perioperative Complications to Cardiac Surgery With Intensive Control of Hyperglycemia

Written by Dennis Bittner

Hyperglycemia is a common condition among cardiac surgery patients, and it occurs in approximately half of all patients following surgery. Although it is agreed that controlling hyperglycemia reduces risk of organ failure, infection, and mortality, the ideal target range for blood glucose (BG) in the perioperative period remains unknown. The 2009 American Diabetes Association (ADA) guidelines recommended a range of 140 to 180 mg/dL BG in intensive care unit (ICU) patients [Moghissi ES et al. *Endocr Pract.* 2009], but the intensive glucose control required to deliver this range results in severe hypoglycemia (<40 mg/dL) in 5% to 20% of ICU patients [Umpierrez et al. *J Clin Endocrinol Metabol*. 2002].

Guillermo Umpierrez, MD, Emory University School of Medicine, Atlanta, Georgia, USA, presented results from the GLUCO-CABG trial [NCT01792830]. The objective of this randomized, controlled study was to determine if intensive glucose control while the patient is in the ICU following coronary artery bypass grafting (CABG) can improve outcomes. The primary end point was a composite end point that included a variety of potential surgical complications. The study included men and women between 18 and 80 years, with or without a history of diabetes, who had undergone CABG with or without valve surgery, and had displayed hyperglycemia (defined as BG>140 mg/dL) either during surgery or during their stay in the ICU. At baseline, patient characteristics were similar between the 2 treatment groups (Table 1).

Patients were randomized to either intensive control of BG (range, 100 to 140 mg/dL) using computer algorithm to guide the infusion of insulin or conservative therapy within the ADA-recommended range (141 to 180 mg/dL). After attrition, a total of 148 patients in each group achieved 80% power for the study to detect an odds ratio of 0.35 in composite outcome ($\alpha = 0.05$).

In the 90 days following hospital discharge, patients treated with intensive glucose control in the ICU had a 42% rate of surgical complications, compared with 52% in patients treated with conservative control (Figure 1). The difference between the 2 groups was not significant, however, on a composite of complications that included death, pneumonia, acute kidney injury (AKI), respiratory

Table 1. Patient Characteristics at Baseline

	Intensive	Conservative	*P* Value
Number of patients	151	151	—
Female/male, n	45/106	39/112	.44
Race, W/B/O	110/35/6	111/34/6	1.00
Age, y	64 ± 9	64 ± 10	.84
BMI, kg/m^2	31 ± 7	30 ± 7	.40
History of DM, n (%)	77 (51)	75 (50)	.82
Duration of DM, y	11 ± 9	11 ± 10	.72
APACHE score	22 ± 3	22 ± 4	.12
BG admission, mg/dL (mmol/L)	140 ± 60 (7.8 ± 3.3)	143 ± 65 (7.9 ± 3.6)	.44

APACHE, Acute Physiology and Chronic Health Evaluation; BG, blood glucose; BMI, body mass index; DM, diabetes mellitus; W/B/O, white/black/other.

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