SCALE Diabetes: Continually Dosed Liraglutide May Aid Weight Loss in T2DM

Written by Lynne Lederman

Ralph DeFronzo, MD, University of Texas Health Science Center, San Antonio, Texas, USA, presented the results of the Effect of Liraglutide on Body Weight in Overweight or Obese Subjects With Type 2 Diabetes trial [SCALE Diabetes; NCT01272232]. This large, multicenter, international trial investigated the efficacy and safety of 56 weeks of treatment with 2 doses of liraglutide, 3.0 and 1.8 mg, compared with placebo, as an adjunct to diet and exercise in inducing and maintaining weight loss in overweight or obese individuals with type 2 diabetes mellitus (T2DM). A 12-week off-medication follow-up period was designed to determine the effect of treatment cessation on safety and efficacy parameters.

Patients included in the SCALE trial had to have T2DM that was treated with diet and exercise and/or 1 to 3 oral antidiabetic drugs, body mass indexes ≥ 27 kg/m^2, and HbA_{1c} levels of 7% to 10%. Patients were to undergo lifestyle interventions, such as a hypocaloric diet and increased physical activity, throughout the duration of the trial and during the 12-week follow-up period when patients were off medication. Baseline characteristics were similar across the treatment groups (Table 1).

Weight loss was greatest during the first 4 to 6 months of treatment and then plateaued through week 56. Liraglutide provided significantly greater reductions in body weight than placebo; about half of patients lost $\geq 5\%$ of body weight, and 20% of patients lost 10% of body weight. After 12 weeks of treatment cessation, weight regain occurred in both liraglutide groups, although mean weight loss from baseline remained significantly greater with liraglutide 3.0 mg than with placebo (–4.7% vs –2.5%, $P < .001$). Liraglutide resulted in statistically significant reductions in HbA_{1c} compared with placebo. Reductions in HbA_{1c} with liraglutide were steep in the initial 12 weeks and were maintained to week 56.

Liraglutide reduced fasting plasma glucose (FPG) and systolic blood pressure (SBP) within the first 2 weeks of treatment. Levels of FPG were maintained for 56 weeks but rapidly returned to baseline after treatment cessation (Table 2).

No patients developed pancreatitis during the study. Lipase and amylase activity increased early in treatment with liraglutide but remained below the upper normal limit and returned to baseline off treatment.

Table 1. SCALE Diabetes Trial Baseline Characteristics

Variable	Liraglutide 3.0 mg	Liraglutide 1.8 mg	Placebo
Randomized individuals, n	423	211	212
Age, y	55.0 (18.0–79.0)	54.9 (25.0–82.0)	54.7 (28.0–78.0)
Male, %	52.0	51.2	45.8
Fasting body weight, kg	105.7 (60.1–199.4)	105.8 (66.8–193.3)	106.5 (65.0–187.9)
BMI, kg/m^2	37.1 (27.0–61.3)	37.0 (27.1–67.6)	37.4 (27.1–67.4)
FPG, mmol/L	8.8 (5.6–17.3)	8.9 (4.2–16.2*)	8.6 (4.9–16.1)
HbA_{1c}, %	7.9 (6.4–10.3)	8.0 (6.7–10.0)	7.9 (6.5–10.1)
Duration of diabetes, y	7.5 (0.4–36.5)	7.4 (0.3–25.9)	6.7 (0.2–28.6)
Hypertension, %	69.3	70.1	68.4
Dyslipidemia, %	69.7	67.8	59.4
History of CV disease, %	16.4	14.8	12.3
Background diabetes therapy, %			
Diet and exercise only	11.2	14.2	9.5
Metformin only	57.5	54.4	59.7
Combination OADs[a]	31.3	31.4	30.8

BMI, body mass index; CV, cardiovascular; FAS, full analysis set; FPG, fasting plasma glucose; OAD, oral antidiabetic drug; SU, sulfonylurea.

Data are presented as mean (range), unless otherwise stated. All randomized individuals or FAS (background diabetes treatment).

[a]Approximately 25% of individuals in each arm were receiving an SU as part of combination OAD therapy.

*On May 1, 2015, 16 2 was changed to 16.2.

Table 2. Observed Mean Changes From Baseline at Week 68

Variable	Liraglutide 3.0 mg vs Placebo	Liraglutide 1.8 mg vs Placebo	Liraglutide 3.0 vs 1.8 mg
Estimated differences in body weight at week 68, %	−2.17 (P = .0002)	−1.20 (P = NS)	−0.97 (P = NS)
Estimated differences in FPG, mmol/L	−0.09 (P = NS)	0.12 (P = NS)	−0.20 (P = NS)
Estimated differences in SBP, mm Hg	−1.36 (P = NS)	−1.72 (P = NS)	0.37 (P = NS)
Estimated difference in pulse, beats/min	−1.92 (P = .0419)	−0.92 (P = NS)	−1.00 (P = NS)

FPG, fasting plasma glucose; NS, not significant; SBP, systolic blood pressure.

Nausea was the most frequently reported side effect and occurred in about 15% of patients. Nausea was more common in patients treated with liraglutide. The incidence was greatest in the first 4 to 8 weeks and then gradually declined.

Liraglutide is not currently approved for weight management; however, in this study, it resulted in greater reductions in body weight in overweight or obese individuals with T2DM than placebo. In the 12 weeks after treatment stopped, patients had increases in weight, although the increases did reach the baseline weight. Benefits in FPG and SBP during treatment were also lost after treatment cessation. This study suggests that liraglutide is well tolerated and results in weight loss and improvements in FPG.

Patient Involvement in Diabetes Care: Greek Study of Decision Aids Inconclusive

Written by Dennis Bittner

The high cost of treatment and large variation in the quality of patient care are major concerns in the treatment of type 2 diabetes mellitus (T2DM) [Halperin F et al. *N Engl J Med*. 2008]. Increasing the degree of patient involvement in decisions related to treatment of their condition has been advocated in current T2DM guidelines [Inzucchi SE et al. *Diabetologia*. 2012] and has been shown to improve the overall quality of care [Stacey D et al. *Cochrane Database Syst Rev*. 2014]. The increased cost of new treatments enables patient involvement, because decisions for optimal individualized treatment become less technical and more value based [Grant RW et al. *Diabetes Care*. 2007]. Tools known as decision aids (DAs) have emerged to facilitate a shared decision-making process between patient and physician [Stacey D et al. *Cochrane Database Syst Rev*. 2014].

Thomas Karagiannis, MD, Aristotle University of Thessaloniki, Thessaloniki, Greece, presented a poster with preliminary results from the multicenter, cluster-randomized Diabetes Medication Choice Cards Trial in Greece [NCT01861756; EASD 2014 (poster 1077)] evaluating use of the Diabetes Medication Choice DA, which consists of cards providing a comparison of commonly used antidiabetic medication classes among 7 domains: blood sugar, daily sugar testing, low blood sugar, daily routine, weight change, side effects, and cost.

The objective of the study was to implement the DA (originally developed by the Mayo Clinic), assess its efficacy in patients with T2DM in primary and secondary care practices throughout Greece, and compare it with usual care. Practices were matched based on type of setting (urban or rural) and level of care (primary or secondary) before randomization of patients to either use of the Diabetes Medication Choice DA or usual care.

Patients eligible for the study were adults who had been diagnosed with T2DM at least 1 year, had more than 1 treatment option available, and were able to both provide informed consent and participate in decision making for their treatment. Patient characteristics were balanced between the 2 treatment arms. A total of 5 practices with 101 patients were allocated to the DA, and 4 practices with 103 patients were allocated to usual care. The study consisted of an initial encounter and 2 follow-up visits at 12 and 24 weeks. The quality of the decision-making process was evaluated immediately after the initial encounter by means of a 13-item Decisional Conflict Scale (DCS). Transfer of knowledge to the patient about antidiabetic medications as well as the level of satisfaction of both the patient and clinician were also assessed.

None of the trial results reached statistical significance (Table 1). Although patients in the DA arm displayed lower levels of overall decisional conflict (mean difference, 7.0; 95% CI, −8.1 to 22.2; P = .31), knowledge transfer was high in both groups (mean difference, 2.4%; 95% CI, −16.0 to 20.7; P = .77), and patients allocated to the DA and usual care were equally satisfied.

In the majority of cases, clinicians who had used the DA said that they found the tool to be useful and that it was easy to use and to integrate within their clinical setting.