–1.5) for the empagliflozin–25 mg group. Both treatment groups differed significantly from the placebo group (both, $p < .001$).

There was a small but statistically significant increase in high-density lipoprotein cholesterol for the empagliflozin treatment groups, as well as total cholesterol, compared to placebo. Lipid parameters are summarized in Table 2.

The proportion of patients reporting ≥ 1 adverse events was similar in the treatment groups. The researchers concluded that the use of 10 or 25 mg of empagliflozin as an add-on to metformin therapy for 76 weeks is well tolerated and produces significant and sustained reductions of $HbA_{1c,}$ body weight, and systolic blood pressure compared with placebo in patients with T2DM.

Liraglutide Improves Body Weight, Prediabetes in Overweight and Obese Patients Without T2DM

Written by Emma Hitt Nichols, PhD

Overweight and obese patients without type 2 diabetes mellitus (T2DM) who were treated with liraglutide experienced a greater reduction in body weight and were more likely to revert to normoglycemia compared to those treated with placebo. Xavier Pi-Sunyer, MD, MPH, Columbia University, New York, New York, USA, presented data from a poster on the Effect of Liraglutide on Body Weight in Nondiabetic Obese Subjects or Overweight Subjects With Comorbidities—Obesity and Prediabetes trial [SCALE; NCT01272219].

Obesity is associated with prediabetes, which substantially increases the risk of developing T2DM and related complications [Kasuga M. *J Clin Invest* 2006]. The SCALE trial was designed to evaluate the safety and efficacy of liraglutide on weight management. The purpose of this analysis was to evaluate the effect of liraglutide on weight loss and measurements of diabetes, including fasting and postload glucose, as well as the prevalence of prediabetes and the onset of T2DM.

In the double-blind multicenter Phase 3 SCALE trial, 3731 patients without T2DM who were overweight or obese and had a body mass index (BMI) ≥ 27 kg/m² and ≥ 1 comorbidity were randomly assigned to receive 3.0 mg of subcutaneous liraglutide or placebo for 56 weeks. Patients who received liraglutide were again randomly assigned to liraglutide or placebo for an additional 12 weeks, while patients receiving placebo remained on it. All patients were followed for an additional 2 weeks.

Patients aged ≥ 18 years were eligible for the SCALE trial if they had a BMI ≥ 30 kg/m² or ≥ 27 kg/m² plus dyslipidemia or hypertension (treated or untreated) and stable body weight with a history of failed dietary effort to reduce it. Exclusion criteria were $HbA_{1c} \geq 6.5\%$, fasting plasma glucose ≥ 126 mg/dL, or a 2-hour postchallenge plasma glucose ≥ 200 mg/dL at baseline. All patients were counseled to reduce their caloric consumption by 500 kcal/day and to start an exercise program.

Patients who had received liraglutide experienced a decrease in body weight of 8.0% (8.4 kg) over 56 weeks, compared with 2.6% (2.8 kg) in patients who received placebo, with an estimated treatment difference of –5.4% (–5.6 kg; 95% CI, –5.8% to –5.0%; $p < .0001$). In addition, a greater number of patients in the liraglutide arm experienced a weight loss over 56 weeks of ≥ 5% (estimated OR [EOR], 4.8; 95% CI, 4.1 to 5.6; $p < .0001$) and > 10% (EOR, 4.3; 95% CI, 3.5 to 5.3; $p < .0001$) compared with patients in the placebo arm.

Patients who had received liraglutide and were then randomly reassigned to placebo during the additional 12 weeks experienced weight gain compared with those who remained on liraglutide (estimated treatment difference, 2.2%; $p < .0001$). Liraglutide treatment improved fasting and postload glycemia compared with placebo, as measured by an oral glucose tolerance test, with patients with prediabetes experiencing a greater improvement than those without it.

At 56 weeks, 20.7% of patients in the placebo arm had progressed from normoglycemia to prediabetes compared with 7.2% of patients in the liraglutide arm (EOR, 3.3; logistic regression, $p < .0001$). Furthermore, 69.2% of patients in the liraglutide arm with prediabetes at baseline reverted to normoglycemia at 56 weeks, compared with 32.7% of the placebo arm (EOR, 4.85; $p < .0001$).

More patients in the placebo arm developed T2DM compared with patients in the liraglutide arm (14 vs 4, respectively; EOR, 8.06; $p = .0003$). During the additional 12 weeks, patients randomly reassigned to placebo developed prediabetes more frequently compared with patients who remained on liraglutide.

Dr. Pi-Sunyer indicated that, in his opinion, the data from this analysis of the SCALE trial suggest that the addition of liraglutide to diet and exercise resulted in superior improvements in the prevalence of prediabetes, T2DM, and body weight compared with placebo.