Table 1. Baseline Characteristics of Patients Receiving Lorcaserin BID or Placebo, Mean ± SD

| | Lorcaserin BID[a] (n = 256) | Placebo[a,b] (n = 252) |
|---|---|---|
| Age, y | 53.2 ± 8.3 | 52.0 ± 9.3 |
| Body mass index, kg/dL | 36.1 ± 4.5 | 35.8 ± 4.5 |
| Fasting plasma glucose, mg/dL | 163.3 ± 48.3 | 160.0 ± 41.6 |
| $HbA_{1c}$, % | 8.1 ± 0.83 | 8.1 ± 0.84 |
| Fasting plasma insulin, μIU/mL | 15.0 ± 10.0 | 16.2 ± 14.7 |
| Triglycerides, mg/dL | 172.1 ± 103.6 | 163.5 ± 87.5 |

Each treatment was administered in conjunction with diet and exercise. Significant reductions ($P<.001$) in body weight in the lorcaserin-treated patients were evident starting at week 4 and thereafter to week 52.

[a]N values apply to age and $HbA_{1c}$ only (safety population). For other parameters, the MITT population is presented.

[b]The published abstract reports 253 patients randomized to placebo; the safety population presented here, however, reports the 252 treated patients in the placebo group.

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Overweight Management in Diabetes Mellitus study [BLOOM-DM; NCT00603291], concerning the effects of the weight loss drug lorcaserin in patients with type 2 diabetes mellitus (T2DM) who are overweight or obese.

About 85% of Americans with T2DM are overweight or obese [Centers for Disease Control and Prevention. *Morb Mortal Wkly Rep.* 2004]. Sustained weight reduction of 3% to 5% is advantageous in improving glycemic control [Jensen MD et al. *Circulation.* 2014; Wing RR et al. *Diabet Care.* 2011]. Lorcaserin is a selective 5-$HT_{2c}$ receptor agonist that acts to decrease food consumption and promote satiety, and it has been approved for weight loss in conjunction with diet and exercise.

In the 52-week BLOOM-DM trial, obese and overweight T2DM patients were randomized 1:1:1 in a double-blind manner to placebo, lorcaserin–10 mg QD, or lorcaserin–10 mg BID, in conjunction with a calorie-reduced diet and exercise. Significant reductions versus placebo were evident in $HbA_{1c}$ and fasting plasma glucose levels in patients receiving lorcaserin BID [O'Neil PM et al. *Obesity.* 2012].

The present post hoc analysis involved patients who were randomized to either placebo or lorcaserin BID, who received ≥1 dose of study drug, and whose post-baseline weight was measured at least once—that is, the modified intention-to-treat population. This retrospective analysis aimed to evaluate the putative weight-loss independent effects of lorcaserin on $HbA_{1c}$, fasting plasma glucose, and fasting plasma insulin.

The baseline characteristics of patients treated with placebo or lorcaserin BID were comparable (Table 1).

Patients receiving lorcaserin BID displayed significant reductions ($P<.001$) in fasting plasma glucose when compared with the placebo group, beginning at week 2 and continuing through to week 52. The drop in glucose levels preceded any significant weight loss. A similar pattern of glucose reduction was also evident among a subgroup of patients who did not lose weight while on lorcaserin treatment and who were therefore considered nonresponders (defined as weight loss ≥ 5% at 12 weeks).

Reductions in $HbA_{1c}$ were significantly greater in the lorcaserin-treated group as compared with the placebo group starting at week 12 (first measurement of $HbA_{1c}$) throughout week 52. A similar pattern of reduction in $HbA_{1c}$ was evident in the nonresponder group, even though no changes in body weight occurred. Mean changes in fasting plasma insulin from baseline were not significantly different in patients treated with lorcaserin BID and placebo.

Examination of 256 patients receiving lorcaserin BID and 252 receiving placebo revealed increased treatment-related adverse events of hypoglycemia (29.3% vs 21.0%), headache (14.5% vs 7.1%), back pain (11.7% vs 7.9%), cough (8.2% vs 4.4%), and fatigue (7.4% vs 4.0%).

These post hoc observations of a significant lorcaserin-mediated reduction in fasting plasma glucose and $HbA_{1c}$ before or in the absence of significant weight loss suggest that lorcaserin might affect glucose homeostasis, at least in part, independently from weight loss. Further prospective randomized clinical trials are needed to confirm these observations.

## Liraglutide Helps Achieve Significant Weight Loss in Overweight or Obese Patients

Written by Brian Hoyle

Ken Fujioka, MD, Scripps Clinic, La Jolla, California, USA, reported results of the Effect of Liraglutide on Body Weight in Non-diabetic Obese Subjects or Overweight Subjects With Co-morbidities study [SCALE; NCT01272219], a 56-week randomized, double-blind, placebo-controlled trial demonstrating the efficacy of liraglutide in inducing and maintaining weight loss, and enhancing health-related quality of life (HRQOL), in 3751 obese or overweight patients with or without prediabetes.

The diminished QOL attributable to obesity can be improved by weight loss [Warkenten LM et al. *Obesity Res.* 2014; Ul Haq et al. *Obesity.* 2013]. Liraglutide is a long-acting glucagon-like peptide-1 agonist approved by the Food and Drug Administration for the treatment

of type 2 diabetes, and it also decreases appetite and helps maintain a lower body weight. The primary objective of SCALE was to examine the efficacy of liraglutide (3.0 mg) as compared with placebo on weight loss throughout 56 weeks. Secondary objectives included patient-reported HRQOL outcomes of health status, impact of weight on QOL, and effect of prescription anti-obesity medication.

Inclusion criteria were body mass index (BMI) ≥30 kg/m$^2$ or ≥27 kg/m$^2$ in those with comorbidities, stable body weight, and the prior failure of a weight loss diet.

Patients with or without prediabetes were randomized 2:1 to liraglutide 3.0 mg/day (n = 2487; achieved in a 4-week period of dose escalation) or placebo (n = 1244). After 52 weeks, those without prediabetes were randomized 1:1 to continued liraglutide therapy or placebo for another 18 weeks. Those with prediabetes continued the original randomized treatment through 172 weeks. The present data are from the first 52 weeks of the study, which was the period of identical treatment for those with and without prediabetes.

Patients receiving liraglutide and placebo were comparable at baseline in terms of mean age, gender, mean body weight, mean ranges of BMI defining overweight and categories of obesity, race or ethnicity, prevalence of hypertension and/or dyslipidemia, prior cardiovascular disease, and diagnosis of prediabetes.

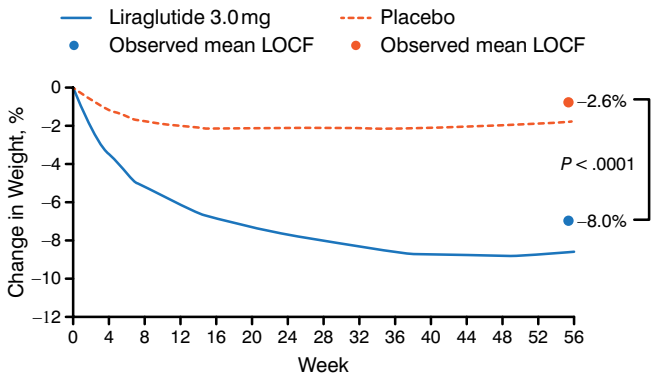
The mean weight loss from baseline to week 56 was significantly greater in those receiving liraglutide than in the placebo group (–8.0% vs –2.6%; $P < .0001$; Figure 1).

In addition, liraglutide led to significant improvements in overall physical health and function, general health, body pain, overall mental health, social functioning, mental health, vitality, self-esteem, sexuality, and work performance. Overall, the odds ratio of a better outcome for liraglutide treatment vs placebo was 1.6 (95% CI, 1.4 to 1.9; $P < .0001$).

Other patient-reported outcomes of the influence of liraglutide treatment indicated that the medication was associated with improved weight management but also had side effects. Adverse effects that occurred in ≥5% of patients included nausea (which persisted throughout the 56 weeks), diarrhea, constipation, vomiting, loss of appetite, and dyspepsia. A variety of other adverse effects were seemingly not related to liraglutide use because they occurred with comparable frequencies in both groups (Table 1).

Despite the inconveniences of the drug-related side effects, the researchers concluded that liraglutide 3.0 mg used as an adjunct to diet and exercise is a means of achieving significant weight loss, and confers patient-related improvements in physical and mental health.

Figure 1. Mean Weight Loss




LOCF, last observation carried forward.

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Table 1. Adverse Events Occurring in ≥5% of Patients

| | Liraglutide 3.0 mg, % | Placebo, % |
|---|---|---|
| Nausea | 40.2 | 14.7 |
| Diarrhea | 20.9 | 9.3 |
| Constipation | 20.0 | 8.7 |
| Vomiting | 16.3 | 4.1 |
| Decreased appetite | 10.8 | 3.1 |
| Dyspepsia | 9.5 | 3.1 |
| Abdominal pain (upper) | 5.7 | 3.5 |
| Abdominal pain | 5.2 | 3.5 |
| Nasopharyngitis | 17.2 | 18.8 |
| Upper respiratory tract infection | 8.6 | 9.8 |
| Influenza | 5.8 | 5.3 |
| Sinusitis | 5.2 | 5.9 |
| Headache | 13.2 | 12.4 |
| Fatigue | 7.5 | 5.2 |
| Dizziness | 6.7 | 4.8 |
| Hypoglycemia[a] | 11.9 | 3.3 |
| Back pain | 6.9 | 8.5 |
| Injection site hematoma | 5.7 | 7.5 |
| Arthralgia | 5.0 | 5.7 |

[a]Based on all events, including those spontaneously reported, and plasma glucose levels at fasting and the Oral Glucose Tolerance Test.

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