Weight loss drug shows positive effect on diabetes

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At the 2018 Meeting of the European Association for the Study of Diabetes, Brigham and Women's Hospital investigators from the Thrombolysis in Myocardial Infarction (TIMI) Study Group presented

diabetes-related findings from CAMELLIA-TIMI 61, a clinical trial of overweight and obese patients designed to test lorcaserin, a weight loss drug manufactured by the trial's sponsor, Eisai Inc. In addition to reporting sustained weight loss without an increased risk of major cardiovascular events, the TIMI Study Group also presented data showing that lorcaserin reduced the risk of diabetes by 19 percent in patients with pre-diabetes, induced remission of hyperglycemia in patients with diabetes, and reduced the risk of diabetic microvascular complications such as microalbuminuria. The team's findings are detailed in a paper published simultaneously in *The Lancet.*

"We recently presented findings showing that use of lorcaserin resulted in modest but sustained weight loss among obese and overweight patients without increasing risk of heart attack and stroke," said co-lead author Erin Bohula, MD, DPhil, a BWH cardiovascular medicine specialist and a staff investigator for the TIMI Study Group at BWH. "Now we report that, when added to lifestyle interventions, lorcaserin significantly reduced incidence of diabetes, increased rates of diabetes remission, and reduced the risk of diabetic microvascular complications."

"Taken together, these findings reinforce the notion that modest, durable weight loss can improve cardiometabolic health and supports the role of lorcaserin as an adjunctive therapy in chronic weight management," said co-lead author Benjamin Scirica, MD, a cardiovascular medicine specialist at BWH and senior investigator for the TIMI Study Group. "It provides another tool in the armamentarium, beyond diet and exercise, for patients hoping to achieve and maintain weight loss. And, happily, as we saw, even relatively modest weight loss can improve the diabetes control in those with diabetes and reduce the development of diabetes in those at risk."

In the Cardiovascular and Metabolic Effects of Lorcaserin in Overweight and Obese Patients-Thrombolysis in Myocardial Infarction

61 (CAMELLIA-TIMI 61) Trial, 12,000 overweight or obese patients at risk for a cardiovascular event were randomly assigned to receive either lorcaserin or a placebo. Patients were followed for a median time of more than three years. At the start of the trial, more than half of participants had diabetes and another third had prediabetes.

Among patients with prediabetes, lorcaserin reduced the risk of diabetes by 19 percent compared to the placebo (172 out of 2,015 patients taking lorcaserin developed diabetes versus 204 out of 1,976 taking the placebo). In addition, 9.2 percent of patients with prediabetes taking lorcaserin were able to achieve normal glycemic levels compared to 7.6 percent of patients taking the placebo (185 out of 2,015 vs. 151 out of 1,976). Lorcaserin also significantly increased the rate of remission of hyperglycemia in patients with diabetes, with 7.1 percent of patients on the drug achieving remission compared to 6 percent of patients on the placebo (242 out of 3,385 vs. 206 out of 3,431).

Lorcaserin also reduced the risk of diabetic microvascular complications, which included persistent microalbuminuria, diabetic retinopathy or diabetic neuropathy, by 21 percent in patients with diabetes.

Patients enrolled in the study had well-controlled diabetes at the trial's start, but lorcaserin still resulted in a net decrease in hemoglobin A1c levels (a measure of glucose control).

Hypoglycemia—dangerously low levels of blood sugar—were reported in 223 (6.6 percent) of the patients with diabetes who received lorcaserin compared with 199 (5.8 percent) who received placebo. In patients on insulin or a sulfonylurea, medications known to result in hypoglycemia, there were numerically more events of severe hypoglycemia requiring hospitalization or considered to be life-threatening with lorcaserin (12 events with lorcaserin vs. 4 events with placebo; p-value non-significant).

The authors note that this finding highlights the importance of carefully titrating agents known to increase risk of hypoglycemia, especially while a patient is working to lose weight.

As previously reported, on top of lifestyle counseling, lorcaserin helped patients lower their weight by 4.2 kilograms (9.3 pounds) on average compared to 1.4 kilograms (3 pounds) for placebo at one year. Significantly more patients taking lorcaserin had lost at least 5 percent of their body weight (39 percent of the lorcaserin group vs. 17 percent of the placebo group) or at least 10 percent of their body weight (15 percent vs. 5 percent) at one year. Differences remained statistically significant through the length of the trial.

"Given the global prevalence of obesity and its association with type 2 diabetes and complications that can cause death or greatly diminish quality of life, we need therapeutic strategies that can be added to lifestyle modification to prevent and control diabetes," said Scirica. "This rigorous and large-scale randomized study demonstrates the potential for improving glycemic control when adding a weight loss agent to a treatment plan."

More information: *The Lancet* (2018). www.thelancet.com/journals/lan … (18)32328-6/fulltext

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