# New drugs line up to challenge Ozempic, Wegovy for weight loss

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After drugmaker Novo Nordisk tweaked its diabetes drug Ozempic into

Wegovy—a formulation expressly designed to help users shed pounds—sales of both drugs skyrocketed.

Other pharmaceutical giants took notice, and over the past weekend the results of multiple clinical trials from would-be competitors were unveiled at this year's annual meeting of the American Diabetes Association (ADA).

Published simultaneously in *The Lancet* and the *New England Journal of Medicine,* trials of two diabetes drugs from Eli Lilly—Mounjaro, an injected drug which is already available to patients, and orforglipron, still in clinical trials—each showed effectiveness in helping users drop pounds.

Also presented at the meeting and published in *The Lancet,* Novo Nordisk released the results of a trial of its new investigational drug, dubbed CagriSema, which contains semaglutide (Ozempic) plus a newer medication, cagrilintide. In that trial, the drug helped people with type 2 diabetes shed excess weight.

## Orforglipron

Lilly's experimental drug orforglipron comes from the blockbuster class of diabetes/weight-loss meds called glucagon-like peptide-1 agonists (GLP-1 agonists) that include Ozempic and Wegovy. However, unlike the latter two drugs, orforglipron is administered as a once-a-day pill rather than an injection, which should make it much more attractive to users.

In one phase 2 trial, published online June 23 in the *New England Journal of Medicine,* 272 adults with overweight or obesity but without a diagnosis of type 2 diabetes were randomly assigned to receive either a placebo or one of four doses of orforglipron (12, 24, 36, or 45

milligrams) daily for nine months. The trial was double-blinded, meaning that neither the study participants nor the trial administrators knew whether or not a particular participant was receiving orforglipron or a placebo.

The result: "A weight reduction of at least 10% by week 36 occurred in 46% to 75% of the participants who received orforglipron [based on dosage], as compared with 9% who received placebo," wrote a team led by Dr. Sean Wharton, of the Wharton Medical Clinic in Burlington, Ontario, Canada. Side effects—"gastrointestinal events, which were mild to moderate"—caused between 10% and 17% of people using orforglipron (depending on the dosage they received) to stop the drug, the study authors noted.

The results of a second phase 2 trial of orforglipron, led by Dr. Juan Frias, of Velocity Clinical Research in Los Angeles, were published online June 24 in *The Lancet.* Participants were recruited from clinics in the United States and Eastern Europe.

This time, 303 patients with type 2 diabetes received either orforglipron, the standard diabetes drug dulaglutide (Trulicity) or a placebo in a double-blinded fashion for 26 weeks. Besides improving participants' blood sugar control, by the end of the trial people taking the 45 mg dose of daily orforglipron lost an average of just over 22 pounds, compared to an average 8.6 pounds for those on dulaglutide and just under 5 pounds for folks on a placebo.

Gastrointestinal issues occurred more often for people taking orforglipron compared to dulaglutide or placebo, with anywhere from 44% to just over 70% of users complaining of such issues, depending on the dosage of orforglipron they were taking.

Both trials were funded by the drug's maker, Eli Lilly.

## Mounjaro

Mounjaro (tirzepatide), another Lilly diabetes drug with results presented at the ADA meeting, has long been approved and available to patients. Like Ozempic, it's given as a once-weekly injection.

The new company-funded clinical trial involved 938 adults living with both type 2 diabetes and overweight/obesity. Patients were randomly assigned to receive Mounjaro or a placebo and weight-loss outcomes were followed for 18 months.

According to a news release from the ADA, "Participants [taking Mounjaro] lost an average of 15% of their starting body weight after 72 weeks of treatment. The overall average weight reduction in patients using tirzepatide was 14.8 kilograms, or 33 pounds."

Gastrointestinal side effects did occur for some patents, but according to the researchers, this resulted in drug discontinuation in less than 5% of cases.

"With a new drug like tirzepatide, it becomes clear we need a weight-centric approach to treating type 2 diabetes when obesity is also present, two conditions that are interwoven for so many Americans," study author Dr. W. Timothy Garvey, director of the Diabetes Research Center at the University of Alabama at Birmingham, said in the ADA news release. "We are encouraged by these weight loss and glycemic control results, especially as weight loss interventions are typically less effective in patients in diabetes."

## CagriSema

Not to be left out, Novo Nordisk, the maker of Ozempic/Wegovy, also

released the results of its new injected weight-loss drug, CagriSema, at the meeting and the findings were published online June 23 in *The Lancet.*

The new medicine contains semaglutide (Ozempic) plus a drug from a different class called cagrilintide. Cagrilintide replicates the action of a natural hormone called amylin, which makes people feel full after eating a meal.

The phase 2 trial was funded by Novo Nordisk and involved 92 overweight or obese patients with type 2 diabetes. All were randomly assigned to receive weekly injections of either CagriSema, cagrilintide alone or semaglutide alone, for eight months.

Blood sugar control was improved with the combo drug versus either drug alone, wrote a team that was also led by Frias.

As for weight loss, by the end of the trial people taking CagriSema lost an average 15.6% of weight, compared to 8.1% taking cagrilintide alone and 5.1% of those taking only semaglutide, Frias' team reported. Rates of "adverse events" (usually gastro issues) were roughly similar across the three groups, affecting about 7 out of 10 participants.

One obesity expert welcomed the news of more potential treatments for obesity.

"I want to highlight how exciting this field is right now. We've never before had medications that have been this effective, so it's really exciting," said Dr. Katherine Saunders, an internist with Weill Cornell Medicine in New York City and a spokeswoman for The Obesity Society. "Obesity is such a complex, heterogeneous disease, so it's not going to be that one medication is the answer for everybody. We need as many tools as we can get in our armamentarium so that we have

effective options for everybody."

**More information:** Find out more about GLP-1 agonist drugs at the Mayo Clinic.