

Amylin plus tirzepatide: Is 23% weight loss the new benchmark?

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People with type 2 diabetes usually lose less weight on incretin drugs than people without it, which has made obesity treatment in this group a persistent gap. New phase 2b data presented at EASD 2026 suggest that adding an amylin agonist to tirzepatide may narrow it, with a mean weight loss of 23.3% at the highest dose over 48 weeks.^{1,2}

KEY TAKEAWAYS

- **The Pivot:** Adding the selective amylin agonist eloralintide to tirzepatide produced mean weight loss of up to 23.3% (24.6 kg) at 48 weeks in adults with obesity or overweight and type 2 diabetes.
- **The Data:** In 367 adults, the 4 combinations lost 13.2% to 23.3% of body weight and cut HbA1c by 2.2 to 2.9 points, against 3.0% and 0.3 points on placebo and 14.8% and 2.4 points on tirzepatide 15 mg alone.
- **The Action:** Treat this as a company-funded phase 2b signal from the efficacy estimand, with no peer-reviewed paper, no published adverse event rates and no long-term data, and wait for phase 3 before changing practice.

Amylin is released alongside insulin from pancreatic beta cells after a meal, and it acts on its own receptor to slow gastric emptying and signal fullness. GIP and GLP-1 are gut hormones released at the same moment, each acting through a separate receptor. Eloralintide is a selective amylin receptor agonist, tirzepatide is a dual GIP/GLP-1 receptor agonist, and Eli Lilly is testing them together as EloraTZP, given as two separate pen injections.¹ Earlier coverage of the amylin class explains why the pathway has drawn so much interest.

The phase 2b study enrolled 367 adults with obesity or overweight and type 2 diabetes, a population in which substantial and sustained weight loss has been hard to achieve. Mean starting weight was 105.4 kg and mean HbA1c was 8.1%. The trial tested 4 combination dose levels against tirzepatide 15 mg alone, 3 eloralintide-only doses and placebo, and ran for 48 weeks.^{1,2}

The Numbers

All 4 EloraTZP dose combinations met the primary endpoint, percent change in body weight versus placebo, and the secondary endpoints, including change in HbA1c. Placebo lost a mean 3.0% of body weight (7.0 lbs) and saw HbA1c fall by 0.3 points. The lowest combination, eloralintide 3 mg plus tirzepatide 5 mg, produced a mean loss of 13.2% (13.9 kg) and an HbA1c fall of 2.2 points.^{1,2}

Weight loss then climbed with dose. Eloralintide 6 mg plus tirzepatide 5 mg reached 19.4%, eloralintide 6 mg plus tirzepatide 10 mg reached 19.9%, and the highest combination, eloralintide 9 mg plus tirzepatide 15 mg, reached 23.3% (24.6 kg, or 54.1 lbs). HbA1c fell by 2.7, 2.6 and 2.9 points respectively. The step from 19.4% to 19.9% when tirzepatide doubled from 5 mg to 10 mg is small, which suggests most of the gain between the lowest and middle doses came from the eloralintide component rather than the tirzepatide dose.²

The single-agent arms give the comparison that matters. Tirzepatide 15 mg alone produced a mean loss of 14.8% and an HbA1c fall of 2.4 points. Eloralintide alone lost 8.2% at 3 mg, 12.3% at 6 mg and 11.1% at 9 mg, with HbA1c falls of 1.1, 1.4 and 1.3 points. The eloralintide-only result plateaus between 6 mg and 9 mg, so the top of the combination range is not simply a bigger dose of one component. The maximum combination sits 8.5 percentage points above tirzepatide 15 mg alone, although the press materials do not report a formal test of that difference, and the primary comparison in the trial was against placebo.²

The lowest combination is worth reading carefully. At 13.2% it sits slightly below tirzepatide 15 mg alone at 14.8%, and its HbA1c fall of 2.2 points is a little smaller than the 2.4 points seen with tirzepatide alone. In other words, adding eloralintide 3 mg to a tirzepatide 5 mg backbone did not match the top tirzepatide dose. The benefit of the combination appears only once eloralintide reaches 6 mg and above, which is where dose selection for any phase 3 programme will matter most.²

All efficacy figures are from the efficacy estimand, which describes results had every randomised participant stayed on their assigned treatment for the full 48 weeks, allowing for dose interruptions and modifications. That is the standard way to describe what a drug can do under ideal adherence, but it is not the same as a treatment-regimen estimand that counts everyone regardless of discontinuation. In a trial where gastrointestinal effects drive dropouts, the two numbers can differ, and a reader should not treat 23.3% as the expected result for every patient who starts treatment.²

Tolerability and What Is Still Unknown

The most common adverse events were gastrointestinal, generally mild or moderate, and occurred mainly during dose escalation. They appeared more often in the combination arms than with eloralintide or tirzepatide alone, which is the expected cost of stacking two agents that both slow gastric emptying and reduce appetite. The press materials give no rates, no discontinuation figures and no serious adverse event counts, so it is not yet possible to say how large that excess is or whether it would limit use outside a trial.²

Several other gaps stand between this result and a treatment decision. The presentation has no abstract, and no peer-reviewed paper exists yet, so the figures come from the EASD press release and the congress presentation itself. There is no reported lean mass or body composition data, no cardiovascular or renal outcome data, and no detail on background diabetes medication, including insulin, which matters because a 2.9-point HbA1c fall in participants on insulin or sulfonylureas would carry a hypoglycaemia risk that the summary does not address.^{1,2}

The study was funded by Eli Lilly, which manufactures eloralintide and tirzepatide. The lead author, Dr Liana K. Billings

of Endeavor Health in Evanston, Illinois, reports consulting honoraria from Novo Nordisk, Amgen, Lilly, Sanofi, Roche and Bayer, and research funding from Novo Nordisk, Amgen, Lilly, Endogenex, Sanofi, Pfizer, AstraZeneca, Roche, Genentech and Kailera in the last 12 months. None of that invalidates the data, but it is the context in which a company-run phase 2b result should be read, particularly before independent replication.²

Dr Billings framed the aim clearly: "We need to continue building on these findings so that, in the future, we can offer patients more treatment options that address both weight and blood sugar control and better reflect the complexity of living with type 2 diabetes and obesity." That is a statement of direction, not of proven benefit. A 48-week phase 2b trial in 367 people can justify a phase 3 programme. It cannot yet tell clinicians how the combination performs in routine practice, in older patients, or in those with advanced kidney or cardiovascular disease.²

CLINICAL IMPLICATIONS

The most useful reading of this result is that amylin adds something tirzepatide does not already provide. The single-agent arms show tirzepatide 15 mg reaching 14.8% and eloralintide alone plateauing near 11% to 12%, while the top combination reaches 23.3%. If those numbers hold up in phase 3, the combination would offer a level of weight loss in type 2 diabetes well beyond what tirzepatide alone delivered in this trial.

For clinicians, the caution is in what the summary leaves out. Gastrointestinal adverse events were more frequent in the combination arms, but the rates are not reported, and giving 2 separate pen injections is a heavier regimen than a single one. Patients on insulin or sulfonylureas will need dose review if HbA1c falls by nearly 3 points, and no data on lean mass has been shared, a point that has become a standing question for every high-efficacy weight loss drug.

Until the full data are published, this is a reason to follow the programme, not a reason to expect a new option soon. A phase 3 trial with a treatment-regimen estimand, reported discontinuation rates and body composition data will show whether the 23.3% figure describes the drug or only the patients who stayed on it.

EDITORIAL & AI STANDARDS

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REFERENCES

1. Billings LK, et al. Phase 2b study of eloralintide combined with tirzepatide (EloraTZP) in adults with obesity or overweight and type 2 diabetes (presentation; no abstract available). Presented at: European Association for the Study of Diabetes (EASD) Annual Meeting; September 28-October 2, 2026; Milan, Italy. No journal publication at the time of writing.
2. European Association for the Study of Diabetes. New investigational drug combining eloralintide and tirzepatide (EloraTZP) led to weight loss of up to 23.3% in people living with obesity and type 2 diabetes. EASD press release (corrected version), September 30, 2026.

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