

Tirzepatide: Efficacy in Weight Management Explored at ATS 2026

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The escalating prevalence of obesity and its associated comorbidities presents a persistent clinical challenge, necessitating effective and sustained therapeutic interventions. Tirzepatide (Zepbound®), a dual glucose-dependent insulintropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, has demonstrated substantial efficacy in chronic weight management, providing a pharmacological option for patients requiring significant weight reduction.

KEY TAKEAWAYS

- **The Pivot:** Tirzepatide offers a dual-agonist mechanism for weight management, distinct from GLP-1 monotherapy.
- **The Data:** Clinical trials have shown mean weight reductions of up to 22.5% from baseline with tirzepatide.
- **The Action:** Clinicians should consider tirzepatide for patients with obesity or overweight with weight-related comorbidities who meet prescribing criteria.

Obesity is a complex, chronic disease associated with numerous adverse health outcomes, including type 2 diabetes, cardiovascular disease, and certain cancers.¹ Lifestyle interventions, while foundational, often prove insufficient for sustained weight loss in many individuals. Pharmacological agents targeting appetite regulation and metabolic pathways are therefore critical components of a comprehensive management strategy. Tirzepatide, approved for chronic weight management in adults with obesity (BMI ≥30 kg/m²) or overweight (BMI ≥27 kg/m²) with at least one weight-related comorbidity, represents a significant advancement in this therapeutic area.² Its mechanism involves agonism at both GIP and GLP-1 receptors, which are enteroendocrine hormones involved in glucose homeostasis and appetite regulation.³ These receptors are found in various tissues, including the pancreas, brain, and gastrointestinal tract, mediating effects such as enhanced insulin secretion, slowed gastric emptying, and reduced food intake. The dual agonism of tirzepatide capitalizes on the synergistic effects of these two incretin pathways, offering a more potent metabolic and weight-reducing effect compared to single-agonist therapies. The global prevalence of obesity has nearly tripled since 1975, affecting over 650 million adults worldwide, underscoring the urgent need for effective and sustainable treatment options.¹

Clinical Efficacy of Tirzepatide

The efficacy of tirzepatide for chronic weight management was primarily established in the SURMOUNT clinical trial program.⁴ The SURMOUNT-1 trial, a phase 3, double-blind, randomised, placebo-controlled study, evaluated tirzepatide in adults with obesity or overweight without type 2 diabetes.⁴ Participants were randomised to receive once-weekly

subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 72 weeks.⁴ The study enrolled 2,539 adults with a mean baseline body weight of 104.8 kg and a mean BMI of 38.0 kg/m². Key exclusion criteria included a history of bariatric surgery, type 1 or type 2 diabetes, or a recent history of cardiovascular events. The primary endpoints were the percentage change in body weight from baseline and the achievement of a body weight reduction of 5% or more.⁴ Results from SURMOUNT-1 demonstrated dose-dependent and statistically significant weight reductions with tirzepatide compared to placebo.⁴ At 72 weeks, the mean percentage change in body weight from baseline was -15.0% with 5 mg tirzepatide, -19.5% with 10 mg, and -20.9% with 15 mg, compared to -3.1% with placebo (P4 A weight reduction of 5% or more was achieved by 85%, 89%, and 91% of participants receiving 5 mg, 10 mg, and 15 mg tirzepatide, respectively, compared to 35% with placebo.⁴ Furthermore, 50%, 62%, and 57% of participants in the 5 mg, 10 mg, and 15 mg groups, respectively, achieved a weight reduction of 20% or more, compared to 3% with placebo.⁴ These substantial weight loss outcomes were accompanied by improvements in cardiometabolic risk factors, including blood pressure, lipid levels, and inflammatory markers, further highlighting the comprehensive benefits of tirzepatide beyond weight reduction.⁴

The SURMOUNT-2 trial extended these findings to adults with obesity or overweight and type 2 diabetes.⁵ This trial also demonstrated significant weight loss, with mean percentage changes in body weight from baseline of -12.8% (10 mg) and -14.7% (15 mg) compared to -3.2% with placebo at 72 weeks (P5 These data underscore the consistent efficacy of tirzepatide across different patient populations, including those with the additional challenge of managing type 2 diabetes, where weight loss can be particularly difficult to achieve.⁵

Adverse events reported in the SURMOUNT trials were predominantly gastrointestinal, consistent with the known class effects of GLP-1 receptor agonists.^{4,5} Nausea, diarrhoea, and constipation were the most common events, generally mild to moderate in severity, and typically occurred during dose escalation.^{4,5} Discontinuation rates due to adverse events were higher in the tirzepatide groups compared to placebo but remained within acceptable ranges for chronic therapy.^{4,5} Strategies for managing these side effects, such as gradual dose titration and patient education, are crucial for improving treatment adherence.

Limitations of the current data include the relatively short duration of the pivotal trials (72 weeks), which does not fully address the long-term sustainability of weight loss or the potential for weight regain after cessation.^{4,5} While the SURMOUNT program provided robust evidence for efficacy, the generalizability of these findings to more diverse real-world populations, including those with severe comorbidities or specific ethnic backgrounds, requires further investigation. The trials also primarily focused on individuals without a history of bariatric surgery, limiting conclusions for this patient group. Further research is ongoing to evaluate the cardiovascular outcomes and extended safety profile of tirzepatide in larger and more diverse populations.⁶ The cost-effectiveness of tirzepatide in various healthcare systems also warrants continued investigation.⁷ Long-term studies are essential to understand the full impact of tirzepatide on obesity-related morbidity and mortality.

CLINICAL IMPLICATIONS

The consistent and substantial weight loss observed with tirzepatide, particularly the proportion of patients achieving 20% or more body weight reduction, represents a meaningful advance in obesity pharmacotherapy. For general practitioners and specialists managing patients with obesity, tirzepatide offers a potent tool that

moves beyond the modest efficacy seen with older agents. The dual GIP/GLP-1 agonism appears to confer an advantage over GLP-1 monotherapy, prompting a re-evaluation of treatment algorithms for patients who have not achieved adequate weight loss with lifestyle interventions or less potent medications.

However, the practicalities of prescribing tirzepatide extend beyond efficacy. The gastrointestinal side effect profile, while generally manageable, requires careful patient counselling and a structured dose escalation. Furthermore, the cost of these novel agents remains a significant barrier for many patients and healthcare systems, raising questions about equitable access. Payers will increasingly scrutinise the long-term benefits, including reductions in obesity-related comorbidities, to justify the investment.

The pharmaceutical industry, specifically Eli Lilly, has clearly positioned tirzepatide as a leader in the burgeoning weight management market. The competitive landscape with other GLP-1 receptor agonists, such as semaglutide, will drive further innovation and potentially broader access. Clinicians should remain informed about head-to-head comparisons and real-world data as they emerge, ensuring that prescribing decisions are based on the most current evidence and individual patient needs, rather than marketing alone.

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REFERENCES

1. World Health Organization. Obesity and overweight. Accessed [Current Date].
2. US Food and Drug Administration. Zepbound (tirzepatide) prescribing information. Accessed [Current Date].
3. Frias JP, et al. Tirzepatide, a dual GIP and GLP-1 receptor agonist, for the treatment of type 2 diabetes. *Lancet*. 2021;397(10269):181-193.
4. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide Once Weekly for the Treatment of Obesity. *N Engl J Med*. 2022;387(3):205-216. doi:10.1056/NEJMoa2206038
5. Garvey WT, et al. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a randomised, double-blind, multicentre, phase 3 trial. *Lancet*. 2023;402(10402):613-626. doi:10.1016/s2213-8587(24)00377-2
6. Eli Lilly and Company. A study of tirzepatide (LY3298176) in participants with obesity or overweight and established cardiovascular disease (SURMOUNT-CVOT). ClinicalTrials.gov Identifier: NCT05556512.
7. Institute for Clinical and Economic Review (ICER). Tirzepatide for Obesity: Effectiveness and Value. Accessed [Current Date].

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