



Tirzepatide: a new treatment for obesity — literature review

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ABSTRACT

Introduction: Obesity is defined by the World Health Organization as “abnormal or excessive fat accumulation that presents a risk to health,” and is frequently associated with type 2 diabetes mellitus and cardiovascular disease. Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have represented a significant advance in pharmacological therapy, demonstrating efficacy in weight reduction and glycaemic control. The combined action of glucose-dependent insulintropic polypeptide (GIP) and GLP-1 led to the development of dual GIP/GLP-1 receptor agonists (twincretins). Tirzepatide was approved in 2022 for glycaemic control in adults with T2DM and subsequently, in 2023, for the treatment of obesity.

Objectives: To critically review the scientific evidence regarding the clinical efficacy and safety profile of tirzepatide in the treatment of obesity in individuals with and without type 2 diabetes mellitus, analysing the main clinical trials and their impact on weight loss.

Methodology: A narrative literature review was conducted between October 2022 and February 2026 using the PubMed, ScienceDirect, b-on, Google Scholar, and ClinicalTrials.gov databases. The terms “Obesity,” “Tirzepatide,” “GIP,” “GLP-1,” “Twincretin,” and “Anti-obesity medication” were used in combination with Boolean operators. Of the 283 articles identified, 56 were selected following relevance assessment and full-text review. Phase III randomized clinical trials published between 2021 and 2025 were included, involving adults with obesity or overweight, with or without T2DM, focusing the analysis on the SURPASS and SURMOUNT (1–5) trial programmes.

Results: In the SURPASS trials, once-weekly tirzepatide (5–15 mg) in individuals with type 2 diabetes mellitus significantly reduced body weight (5–11 kg), HbA1c (up to 2.8%), and improved cardiometabolic parameters. The SURMOUNT programme confirmed robust efficacy in the treatment of obesity. SURMOUNT-1 demonstrated mean weight reductions of 15–22% in individuals without type 2 diabetes mellitus, with a significant proportion achieving ≥20% weight loss. SURMOUNT-2 showed 13–15% reductions in patients with type 2 diabetes mellitus, associated with significant metabolic improvement. SURMOUNT-3 demonstrated additional benefit following intensive lifestyle intervention, reinforcing a complementary effect. SURMOUNT-4 showed weight regain after treatment discontinuation, supporting the need for long-term maintenance therapy. SURMOUNT-5 demonstrated superiority in weight reduction compared with semaglutide 2.4 mg. The safety profile was favourable, with predominantly gastrointestinal adverse

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events that were dose-dependent and mostly mild to moderate. The discontinuation rate was comparable to that observed with other incretin-based therapies.

Conclusion: Tirzepatide represents an innovative and effective therapeutic strategy for the treatment of obesity, achieving weight reductions of 15–22% and consistent metabolic benefits in individuals with and without type 2 diabetes mellitus. The available evidence suggests a clinically meaningful impact and the potential to modify the therapeutic paradigm of obesity management, although additional long-term data are required. A triple GIP/GLP-1/glucagon receptor agonist is also under investigation and may further expand future therapeutic options.
