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# Tirzepatide Once Weekly for the Treatment of Obesity

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## Abstract

**Background:** Obesity is a chronic disease that results in substantial global morbidity and mortality. The efficacy and safety of tirzepatide, a novel glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist, in people with obesity are not known.

**Methods:** In this phase 3 double-blind, randomized, controlled trial, we assigned 2539 adults with a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of 30 or more, or 27 or more and at least one weight-related complication, excluding diabetes, in a 1:1:1 ratio to receive once-weekly, subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 72 weeks, including a 20-week dose-escalation period. Coprimary end points were the percentage change in weight from baseline and a weight reduction of 5% or more. The treatment-regimen estimand assessed effects regardless of treatment discontinuation in the intention-to-treat population.

**Results:** At baseline, the mean body weight was 104.8 kg, the mean BMI was 38.0, and 94.5% of participants had a BMI of 30 or higher. The mean percentage change in weight at week 72 was -15.0% (95% confidence interval [CI], -15.9 to -14.2) with 5-mg weekly doses of tirzepatide, -19.5% (95% CI, -20.4 to -18.5) with 10-mg doses, and -20.9% (95% CI, -21.8 to -19.9) with 15-mg doses and -3.1% (95% CI, -4.3 to -1.9) with placebo ( $P < 0.001$  for all comparisons with placebo). The percentage of participants who had weight reduction of 5% or more was 85% (95% CI, 82 to 89), 89% (95% CI, 86 to 92), and 91% (95% CI, 88 to 94) with 5 mg, 10 mg, and 15 mg of tirzepatide, respectively, and 35% (95% CI, 30 to 39) with placebo; 50% (95% CI, 46 to 54) and 57% (95% CI, 53 to 61) of participants in the 10-mg and 15-mg groups had a reduction in body weight of 20% or more, as compared with 3% (95% CI, 1 to 5) in the placebo group ( $P < 0.001$  for all comparisons with placebo). Improvements in all prespecified cardiometabolic measures were observed with tirzepatide. The most common adverse events with tirzepatide were gastrointestinal, and most were mild to moderate in severity, occurring primarily during dose escalation. Adverse events caused treatment discontinuation in 4.3%, 7.1%, 6.2%, and 2.6% of participants receiving 5-mg, 10-mg, and 15-mg tirzepatide doses and placebo, respectively.

**Conclusions:** In this 72-week trial in participants with obesity, 5 mg, 10 mg, or 15 mg of tirzepatide once weekly provided substantial and sustained reductions in body weight. (Supported by Eli Lilly; SURMOUNT-1 ClinicalTrials.gov number, [NCT04184622](#).)

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PMID: 35657317 No abstract available.

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Dekker TJA.

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