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Tirzepatide for Obstructive Sleep Apnea and Obesity

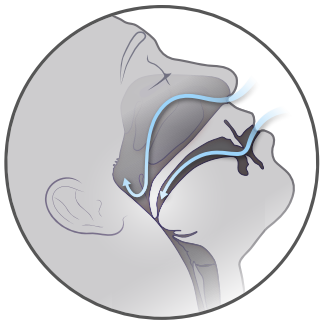
A PLAIN LANGUAGE SUMMARY

Based on the NEJM publication: Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity by A. Malhotra et al. (published June 21, 2024)

In two trials, researchers assessed the efficacy and safety of tirzepatide for the treatment of adults with obstructive sleep apnea and obesity.

Obstructive sleep apnea is characterized by repetitive pharyngeal collapse during sleep, resulting in apneas and hypopneas. It is also an independent risk factor for cardiovascular disease.

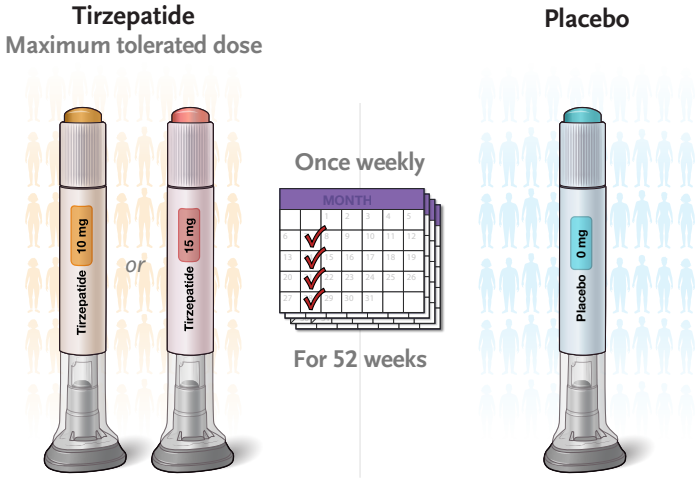
WHY WERE THE TRIALS DONE?



Excess adiposity is a major reversible risk factor for obstructive sleep apnea and its complications. Tirzepatide — a long-acting agonist of the glucose-dependent insulinotropic polypeptide receptor and glucagon-like peptide-1 receptor — has been shown to reduce body weight. Whether tirzepatide can treat obstructive sleep apnea is unknown.

HOW WERE THE TRIALS CONDUCTED?

In two trials, 469 adults with moderate-to-severe obstructive sleep apnea and obesity were assigned to receive the maximum tolerated dose of tirzepatide (10 mg or 15 mg) or placebo subcutaneously once weekly for 52 weeks. Trial 1 enrolled participants who were not receiving positive airway pressure (PAP) therapy. Trial 2 enrolled those who were receiving PAP therapy. The primary end point was the change from baseline in the apnea–hypopnea index (AHI, the number of apneas and hypopneas during an hour of sleep).



PARTICIPANTS

WHO

Trial 1 (no PAP therapy):
234 adults
Mean age, 48 years
Men: 67%; Women: 33%

Trial 2 (PAP therapy):
235 adults
Mean age, 52 years
Men: 72%; Women: 28%

CLINICAL STATUS

Apnea–hypopnea index, at least 15 events per hour (mean, approximately 50)

Body-mass index, at least 30 (mean, 39)

No type 1 or type 2 diabetes

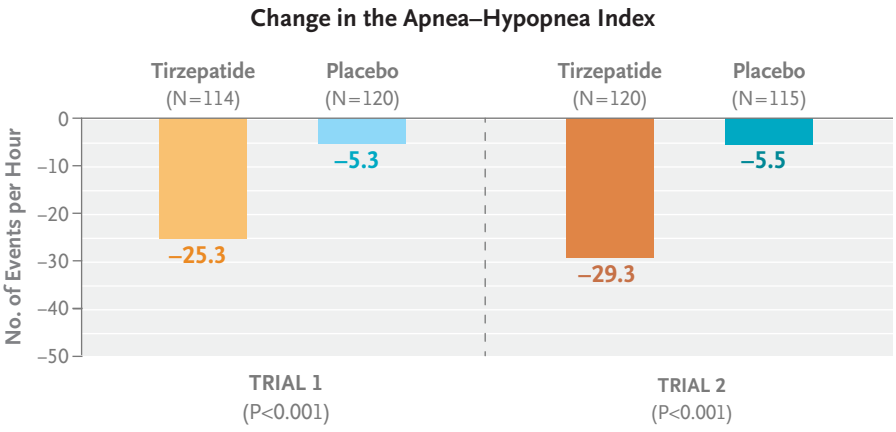
TRIAL DESIGN

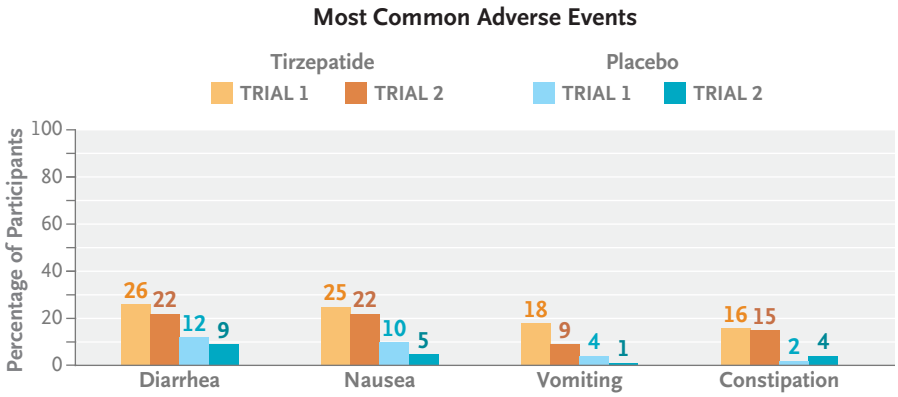
- PHASE 3
- RANDOMIZED
- DOUBLE-BLIND
- PLACEBO-CONTROLLED
- DURATION: 52 WEEKS
- LOCATION: 60 SITES ACROSS 9 COUNTRIES

RESULTS

In both trial 1 and trial 2, tirzepatide led to a significantly greater reduction in the AHI at week 52 than placebo.

All key secondary end points also favored tirzepatide over placebo, including the percent change in body weight and changes in systolic blood pressure and high-sensitivity C-reactive protein concentration.





The most common adverse events with tirzepatide were gastrointestinal; most were mild to moderate in severity.

LIMITATIONS AND REMAINING QUESTIONS

- Long-term cardiovascular outcomes could not be assessed, given the design and relatively short duration of the trials.
- The trials excluded participants who did not have obesity and therefore did not analyze the effect of tirzepatide in people with overweight or normal body-mass index.
- The trials were not designed to assess whether the results differed according to participants' symptoms at baseline.

CONCLUSIONS

In adults with moderate-to-severe obstructive sleep apnea and obesity, tirzepatide given once weekly led to a significantly greater reduction in the apnea–hypopnea index at 52 weeks than placebo.

LINKS: FULL ARTICLE | NEJM QUICK TAKE | EDITORIAL

FURTHER INFORMATION

Trial registration: ClinicalTrials.gov number, NCT05412004

Trial funding: Eli Lilly

Full citation: Malhotra A, Grunstein RR, Fietze I, et al. Tirzepatide for the treatment of obstructive sleep apnea and obesity. N Engl J Med 2024;391:1193-205. DOI: 10.1056/NEJMoa2404881