

# Tirzepatide vs. Semaglutide Once Weekly in Patients with Type 2 Diabetes

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## CLINICAL PROBLEM

Not all patients with type 2 diabetes have adequate glucose control with metformin monotherapy. Tirzepatide is a dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonist under development for treatment of diabetes; how it compares with the selective GLP-1 receptor agonist semaglutide is unknown.

## CLINICAL TRIAL

**Design:** An international, randomized, open-label, phase 3, noninferiority trial was conducted to compare tirzepatide with semaglutide in adults with type 2 diabetes.

**Intervention:** 1879 adults with inadequately controlled diabetes despite metformin treatment were assigned to a once-weekly subcutaneous injection of tirzepatide (5, 10, or 15 mg) or semaglutide (1 mg) for 40 weeks. The primary efficacy end point was the change in glycated hemoglobin level from baseline to 40 weeks.

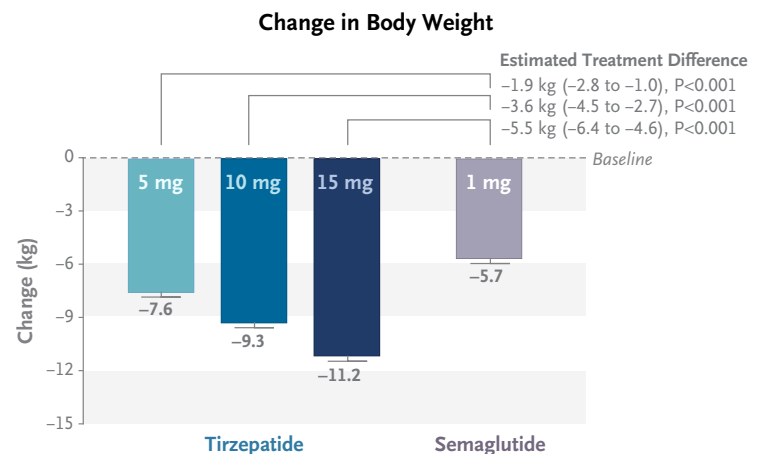
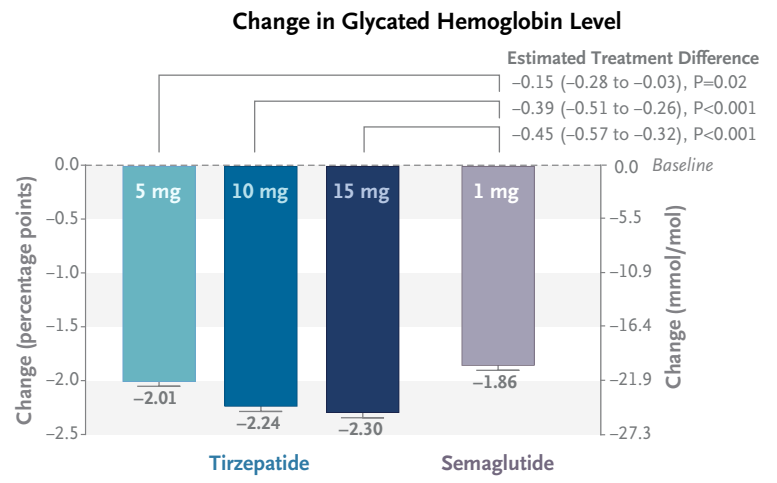
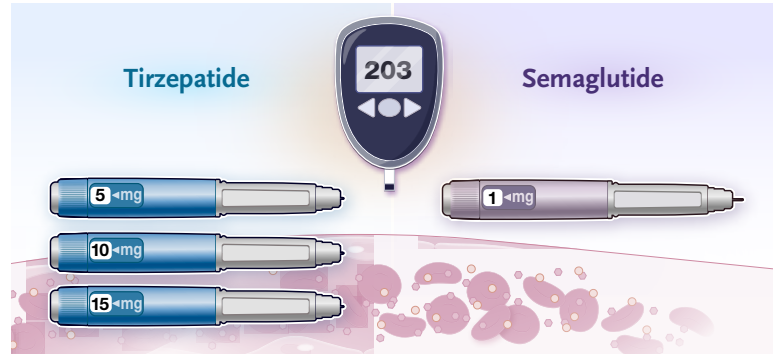
## RESULTS

**Efficacy:** All three tirzepatide doses were noninferior to and also superior to semaglutide with respect to the mean reduction in glycated hemoglobin level. Patients in the tirzepatide groups also lost more weight than those in the semaglutide group.

**Safety:** The percentage of patients reporting any adverse event was similar across the groups, with gastrointestinal events most common. However, serious adverse events were reported by 5.3 to 7.0% of patients in the tirzepatide groups and 2.8% of those in the semaglutide group.

## LIMITATIONS AND REMAINING QUESTIONS

- Treatments were not blinded because of differences in devices and dose-escalation schemes (although individual tirzepatide doses were blinded).
- Higher doses of semaglutide were not compared with tirzepatide.
- Black patients accounted for only 4% of the trial population, so generalizability of the findings is limited.
- How tirzepatide performs in patients with increased cardiovascular risk requires further study.



## CONCLUSIONS

Tirzepatide was noninferior and also superior to semaglutide in reducing glycated hemoglobin levels in adults with type 2 diabetes.