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A Study of Tirzepatide (LY3298176) in Participants With Obesity or Overweight for the Maintenance of Weight Loss

SURMOUNT-4

Efficacy and Safety of Tirzepatide for Maintenance of Weight Loss in Participants Without T2D Who Have Obesity or Overweight With Weight-Related Comorbidities

Study Design

Multicenter

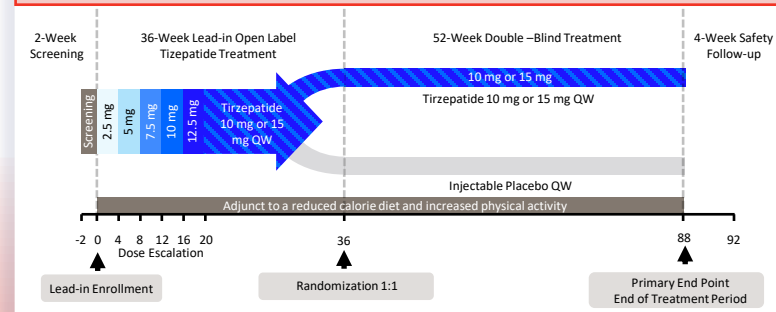
Double-blind

Phase 3

Obesity/ overweight, without T2D

N=670

Interventions



Inclusion Criteria

Age ≥18 years

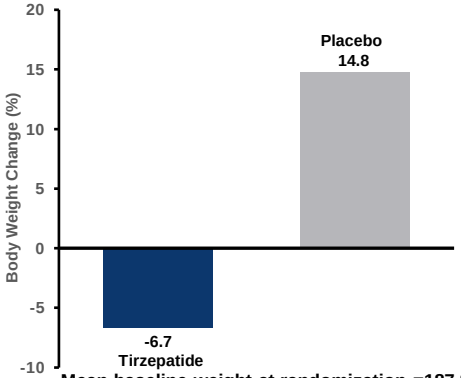
- BMI
  - ≥30 kg/m^2 or
  - ≥27 kg/m^2 and at least 1 weight-related comorbidity[a]

History of ≥1 self-reported unsuccessful dietary effort to lose body weight

Efficacy

Change in Body Weight (%) From Randomization to 88 Weeks (Efficacy Estimand)[b]

Absolute Treatment Difference	-21.4 (-22.9 to -20.0)
P Value	*<.001*

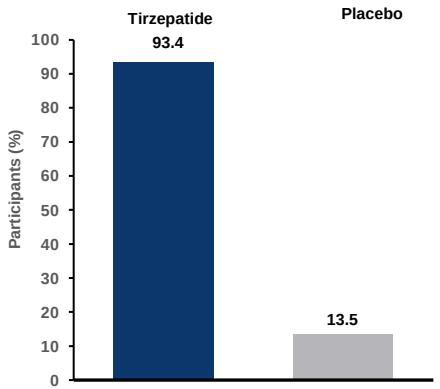


Mean baseline weight at randomization =187.8lb

- Statistically significant difference in weight reduction with maximum tolerated dose compared to placebo during double-blind period
- Participants achieved 21.1% weight loss during a 36-week lead-in treatment period and an additional 6.7% weight loss during a 52-week double-blind treatment period, for a total mean weight loss of 26% over 88 weeks

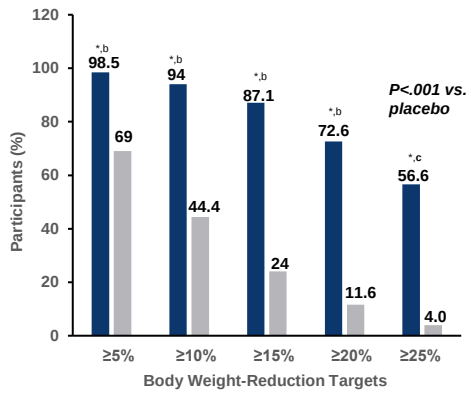
Participants maintaining >=80% body weight loss achieved during lead-in period at week 88 (Efficacy Estimand)[b]

Absolute Treatment Difference	95.9 (54.7 to 168.1)
P Value	*<.001*



A significantly greater proportion of participants continuing maximum tolerated dose maintained ≥80% of the body weight lost during the 36-week lead-in period

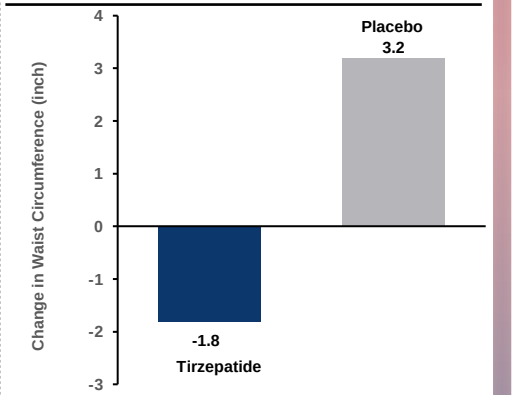
Participants Achieving Body Weight Reduction Targets at Week 88 (Efficacy Estimand)



- Significantly greater proportion of participants on maximum tolerated dose treatment achieved body weight reductions of ≥5%, ≥10%, ≥15% and ≥20% from baseline than placebo
- 56.6% of patients achieved a prespecified exploratory endpoint of ≥25% body weight reduction with maximum tolerated dose

Change in Waist Circumference From Randomization to 88 Weeks (Efficacy Estimand)[b]

Absolute Treatment Difference	-12.9 (-14.1 to -11.7)
P Value	*<.001*



Mean baseline waist circumference=38.4inches

Statistically significant reduction in waist circumference with maximum tolerated dose compared with placebo

Safety

Double-Blind and Safety Follow-Up Period

Overview of AEs; Participants (%)	Tirzepatide (N=335)	Placebo (N=335)
TEAEs	60.3	55.8
SAEs	3.0	3.0
Deaths	0.3	0.3
AEs leading to treatment discontinuation	1.8	0.9
GI AEs (% of participants)		
Diarrhea	10.7	4.8
Nausea	8.1	2.7
Vomiting	5.7	1.2

The most common adverse events occurring with maximum tolerated dose vs placebo were gastrointestinal in nature. These decreased over time in tirzepatide-treated patients during the lead-in period and leveled off during the double-blind period

Conclusion: In this 88-week trial, participants with obesity or overweight, withdrawing tirzepatide led to regain of some lost weight, whereas continued treatment maintained and augmented initial weight reduction.

AE=Adverse Event; BMI=Body Mass Index; GI=Gastrointestinal; QW=Once Weekly; SAE=Serious Adverse Event; TEAE=Treatment-Emergent Adverse Event; T2D=Type 2 Diabetes.
*P<.001; [a]Hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease; [b]Tested for superiority, controlled for Type 1 error; [c]Tested for significant difference, not controlled for Type 1 error.

Aronne LJ, et al. JAMA. 2023;(Accepted).