Sustained Weight Reduction by Thresholds in Adults with Obesity and Prediabetes Treated with Tirzepatide over 176 Weeks (SURMOUNT-1)

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OBJECTIVE

- To determine sustainability of weight reduction in adults with obesity, or overweight, and prediabetes treated with tirzepatide for 176 weeks in a post hoc analysis of the SURMOUNT-1 study

CONCLUSIONS

- In this post hoc analysis of SURMOUNT-1 3-year study, treatment with tirzepatide over 176 weeks in participants with obesity, or overweight, and prediabetes was associated with a longer continuous time spent with weight reduction thresholds ≥5%, ≥10%, ≥15%, and ≥20% vs. placebo
  - In this trial of 176 weeks, those treated with tirzepatide who achieved ≥20% weight reduction sustained that weight reduction for 73-80% (median) of the time in the trial
- Currently, the Phase 3 SURMOUNT-MMO study is evaluating the effect of tirzepatide on morbidity and mortality outcomes in participants with obesity

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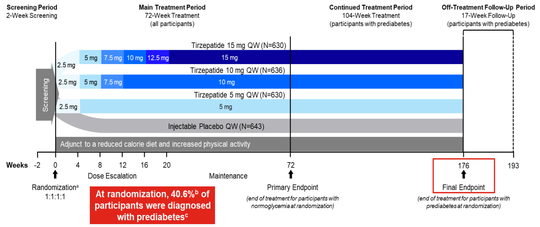
BACKGROUND

- In adults with obesity or overweight, long-term weight reduction is associated with continued reduction in cardiovascular risk and mortality[1]
- Tirzepatide is a once-weekly dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist approved for treatment of adults with type 2 diabetes, obesity, and moderate-to-severe obstructive sleep apnea with obesity[2,3]
- In the Phase 3 SURMOUNT-1 study, treatment with tirzepatide for 72 weeks demonstrated substantial and sustained weight reduction in adults with obesity or overweight with weight-related comorbidities[4]
  - Additionally, among those with prediabetes at baseline, tirzepatide treatment for a total of 176 weeks demonstrated substantial and sustained weight reduction[5]

SURMOUNT-1 STUDY DESIGN

Adults With Prediabetes



[a]Participants with normoglycemia completed the study after 72 weeks of treatment, whereas those with prediabetes completed the study after 176 weeks of treatment; [b]Of the 2539 participants randomized, 1032 were diagnosed with prediabetes, of whom 762 were treated with tirzepatide (5 mg: n=247; 10 mg: n=262; 15 mg: n=253) and 270 were treated with placebo; [c]At randomization, glycemic status was assessed using fasting glucose, HbA1c, and 2-hour OGTT as defined by the 2019 American Diabetes Association guidelines[1]; see Jastreboff AM, et al. N Engl J Med. 2022;387:205-216.

1. American Diabetes Association. Diabetes Care. 2019;42:s13-s28.

Key Eligibility Criteria

Inclusion Criteria

- Adults with obesity (body mass index [BMI] ≥30 kg/m^2), or overweight (BMI ≥27 kg/m^2) with ≥1 weight-related comorbidities[a]
  - Prediabetes at randomization was an eligibility requirement for the 3-year portion of the study

Exclusion Criteria

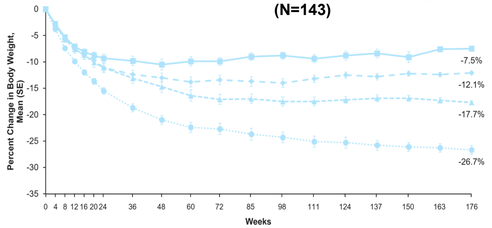
- Diabetes (type 1 or type 2)
- >5-kg body weight change within 90 days before screening
- Prior or planned surgical treatment for obesity
- Treatment that promotes weight loss within 90 days before screening

[a]Hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease.

KEY RESULTS

Participants Treated With Tirzepatide 5 mg Achieved and Sustained Weight Reduction Up to Week 176 Across All Levels of Weight Reduction

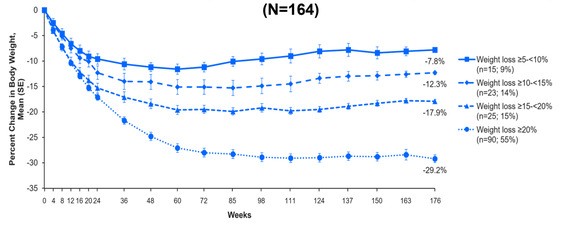
Percent Change in Body Weight by Visit by Weight Reduction Group Based on Week 176 Weight in Participants Receiving Tirzepatide 5 mg (N=143)



Notes: Data based on participants with prediabetes at randomization and with weight measurement available at Week 176 treated with tirzepatide (N=143). Of these, data for participants with a maximum of <5% weight reduction treated with tirzepatide (n=11) were not shown. Data for placebo were not shown due to small patient numbers.

Participants Treated With Tirzepatide 10 mg Achieved and Sustained Weight Reduction Up to Week 176 Across All Levels of Weight Reduction

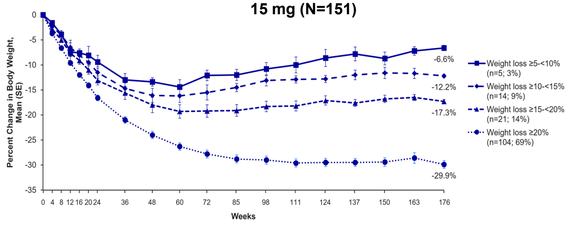
Percent Change in Body Weight by Visit by Weight Reduction Group Based on Week 176 Weight in Participants Receiving Tirzepatide 10 mg (N=164)



Notes: Data based on participants with prediabetes at randomization and with weight measurement available at Week 176 treated with tirzepatide (N=164). Of these, data for participants with a maximum of <5% weight reduction treated with tirzepatide (n=11) were not shown. Data for placebo were not shown due to small patient numbers.

Participants Treated With Tirzepatide 15 mg Achieved and Sustained Weight Reduction Up to Week 176 Across All Levels of Weight Reduction

Percent Change in Body Weight by Visit by Weight Reduction Group Based on Week 176 Weight in Participants Receiving Tirzepatide 15 mg (N=151)



Notes: Data based on participants with prediabetes at randomization and with weight measurement available at Week 176 treated with tirzepatide (N=151). Of these, data for participants with a maximum of <5% weight reduction treated with tirzepatide (n=7) were not shown. Data for placebo were not shown due to small patient numbers.

METHODS

Post Hoc Analysis Population

- This post hoc analysis examined on-treatment data from participants with prediabetes at randomization and with weight measurement available at Week 176 treated with tirzepatide (5 mg: N=143; 10 mg: N=164; 15 mg: N=151) vs. placebo (N=114)

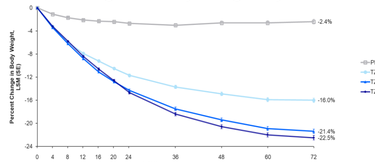
Efficacy

- Sustained weight reduction was defined as achieving a weight reduction of ≥5%, ≥10%, ≥15%, or ≥20% at any point after baseline and maintaining that level of reduction at all subsequent measurements through Week 176
- Weight change over time by weight reduction threshold group was descriptively assessed

Results

SURMOUNT-1 Primary Endpoint[4]

Percent Change in Body Weight by Week



Notes: Data are LSM (SE) and represent the percent change in body weight by weeks since randomization, derived from MMRM analysis for the efficacy estimand. Missing values at Week 72 were imputed from MMRM analysis. The MMRM model for post-baseline measures included baseline value, country, sex, treatment, time, and treatment*time (type III sum of squares) as variables. The ANOVA model for baseline measures include treatment (type III sum of squares) as a variable.

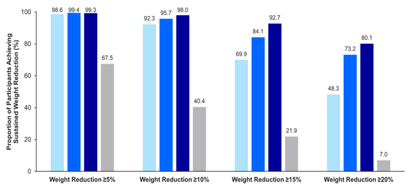
Baseline Demographics and Clinical Characteristics

Characteristic	All Participants (N=2539)[a]	Participants With Prediabetes at Baseline (N=1032)[a]
Age, years	44.9 (12.5)	48.2 (11.8)
Female, n (%)	1714 (67.5)	659 (63.9)
Race, n (%)		
Asian	278 (10.9)	105 (10.2)
Black or African American	201 (7.9)	77 (7.5)
White	1792 (70.6)	758 (73.4)
Hispanic or Latino, n (%)	1214 (47.8)	482 (46.7)
BMI, kg/m^2	38.0 (6.8)	38.8 (7.1)
Weight, kg	104.8 (22.1)	107.3 (23.4)
Waist circumference, cm	114.1 (15.2)	116.5 (15.6)
HbA1c, %	5.6 (0.4)	5.8 (0.3)
Blood pressure, mm Hg		
Systolic	123.3 (12.7)	125.6 (12.7)
Diastolic	78.5 (8.2)	80.6 (8.2)

Note: Data are mean (SD) unless stated otherwise

Higher Proportions of Tirzepatide-Treated Participants Met and Sustained the Defined Weight Reduction Thresholds vs. Participants Randomized to Placebo

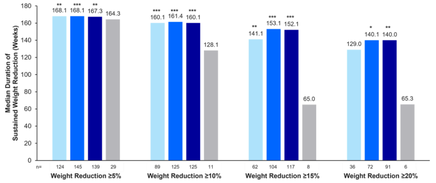
Proportion of Participants Achieving Sustained Body Weight Reduction by Thresholds



Note: Proportions based on on-treatment data from participants with prediabetes at randomization and with weight measurement available at Week 176 treated with tirzepatide (5 mg: N=143; 10 mg: N=164; 15 mg: N=151) vs. placebo (N=114).

Body Weight Reduction Was Sustained for a Longer Period of Time in Tirzepatide-Treated Participants Than Those Randomized to Placebo

Duration of Sustained Body Weight Reduction by Thresholds



*p<0.05, **p<0.01, ***p<0.001 vs. placebo.
Notes: At a given weight reduction threshold, only participants meeting the corresponding sustained weight reduction definition were included.
p-Values comparing each tirzepatide dose vs. placebo were determined using Wilcoxon rank sum test.

References: 1. Khan SS, et al. *JAMA Cardiol.* 2018;3:280-287. 2. MOUNJARO (tirzepatide) [US Highlights of Prescribing Information]. Indianapolis, IN: Eli Lilly and Company, 2024. 3. ZEPBOUND (tirzepatide) [US Highlights of Prescribing Information]. Indianapolis, IN: Eli Lilly and Company, 2025. 4. Jastreboff AM, et al. *N Engl J Med.* 2022;387:205-216. 5. Jastreboff AM, et al. *N Engl J Med.* 2025;392:958-971.

Abbreviations: *ANOVA=analysis of variance; HbA1c=glycated hemoglobin; LSM=least squares mean; MMRM=mixed model for repeated measures; OGTT=oral glucose tolerance test; QW=once weekly; SE=standard error; TZP=tirzepatide.*

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