SURMOUNT-OSA - Study 1
Participants Not on PAP Therapy

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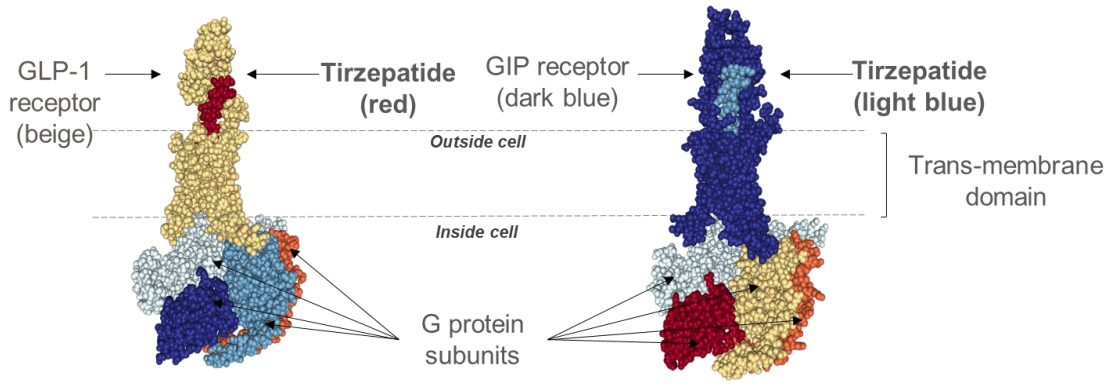
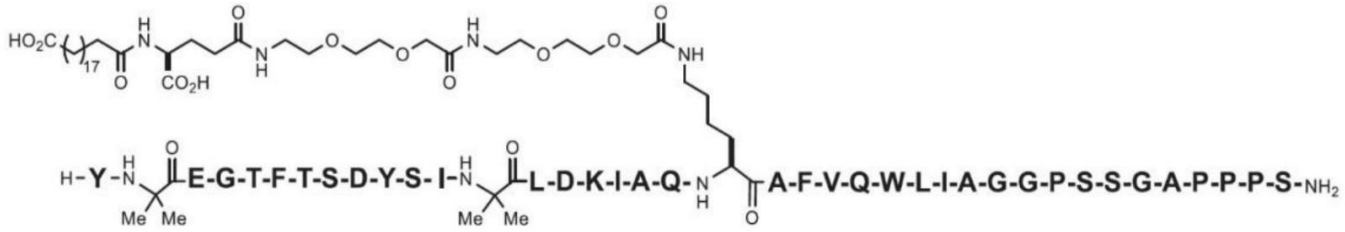
Content Overview

- Tirzepatide
- Study Design
- Key Inclusion and Exclusion Criteria
- Participant Disposition
- Study Endpoints
- Baseline Characteristics
- Results
- Adverse Events
- Summary

Tirzepatide: Molecular Structure and Properties

- Tirzepatide is a long-acting GIP receptor and GLP-1 receptor agonist[1]
- Its amino acid sequence including a C20 fatty diacid moiety that enables albumin binding and prolongs the half-life[1]
- Mean half-life of approximately 5 days (116.7 h), enabling once-weekly dosing[1]
- Its plasma concentrations in patients with renal and hepatic impairment do not differ from those in healthy people[2]





GIP=Glucose-Dependent Insulinotropic Polypeptide; GIPR=Glucose-Dependent Insulinotropic Polypeptide Receptor; GLP-1R=Glucagon-Like Peptide-1 Receptor.

1. Coskun T, et al. *Mol Metab*. 2018;18:3-14. 2. Urva S, et al. *Diabetes*. 2020;69(1):Abstract 971-P.

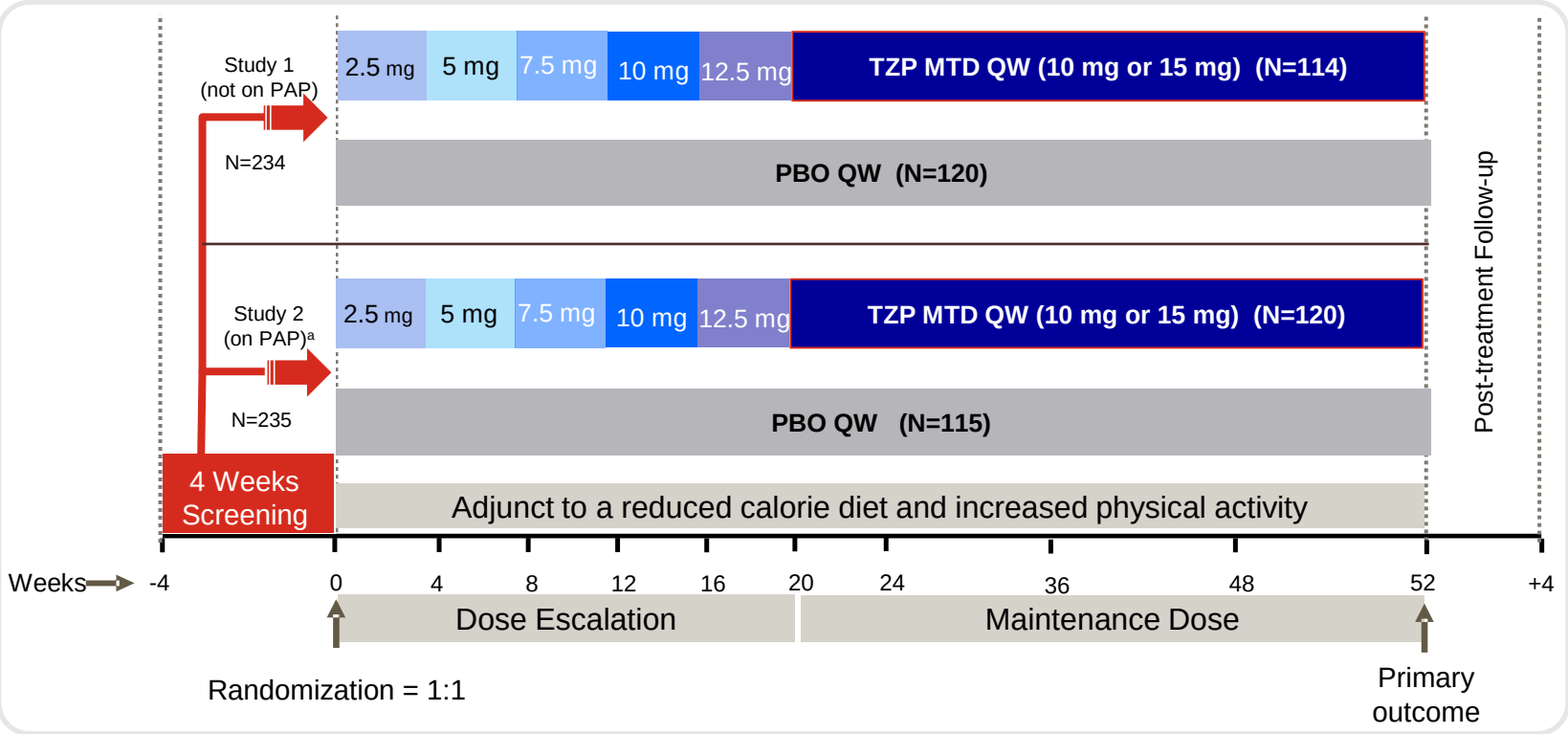
Study Design

Phase 3, 52-week, randomized, double-blind, placebo-controlled master protocol to evaluate the efficacy and safety of TZP at the MTD (10 or 15 mg) vs. placebo as an adjunct to diet and exercise in participants with moderate-to-severe OSA (AHI ≥15 events/hour) and obesity (BMI ≥30 kg/m^2) without T2D[1-3]

Hypothesis:

TZP in people with OSA and obesity will yield important improvements in OSA severity as assessed by the AHI[1,2]

US, Australia, Brazil, China, Czechia, Germany, Japan, Mexico and Taiwan[3]

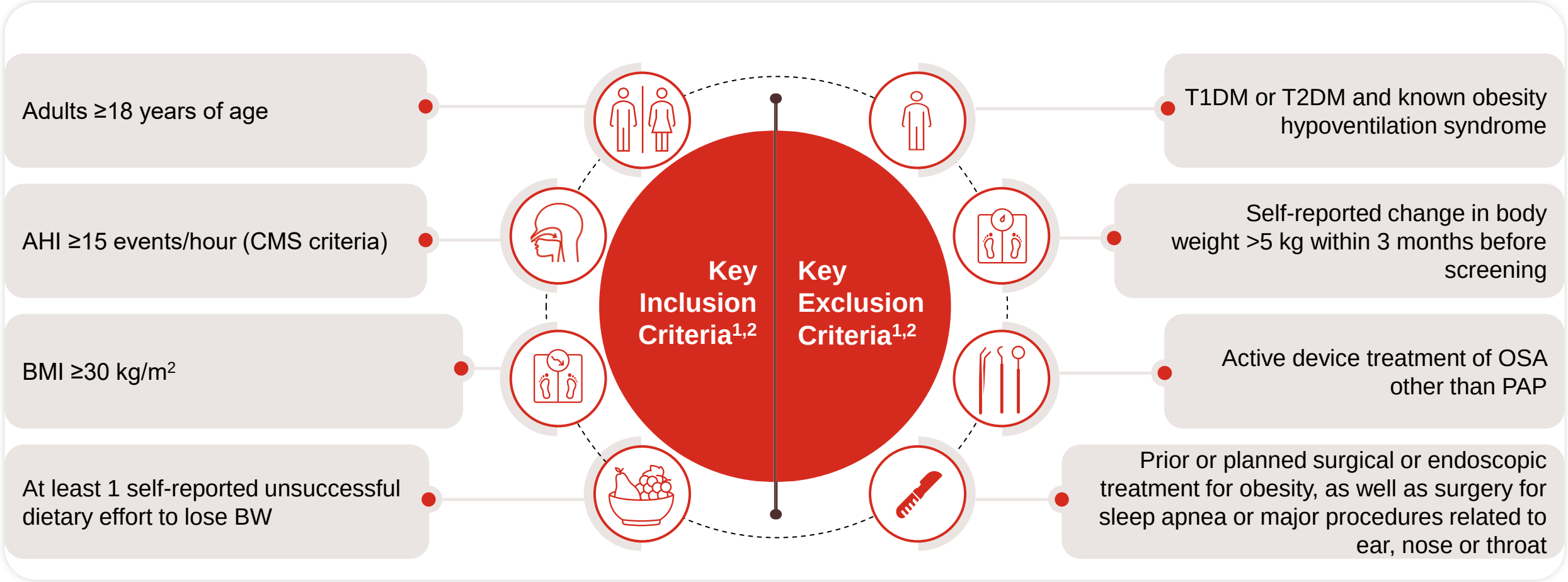


[a]Participants in Study 2 were instructed to suspend PAP therapy for 7 days prior to PSG and PRO assessments at baseline, week 20, and week 52.

AHI=Apnea-Hypopnea Index; BMI=Body Mass Index; MTD=Maximum Tolerated Dose; OSA=Obstructive Sleep Apnea; PAP=Positive Airway Pressure; PBO=Placebo; PRO=Patient Reported Outcomes; PSG=Polysomnography; QW=Once Weekly; R=Randomization; T2D=Type 2 Diabetes; TZP=Tirzepatide.

1. Malhotra A, et al. *Contemp Clin Trials.* 2024;141:107516. 2. https://clinicaltrials.gov/study/NCT05412004 (Accessed April 15, 2024). 3. Malhotra A, et al. *NEJM.* 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

Key Inclusion and Exclusion Criteria of Participants

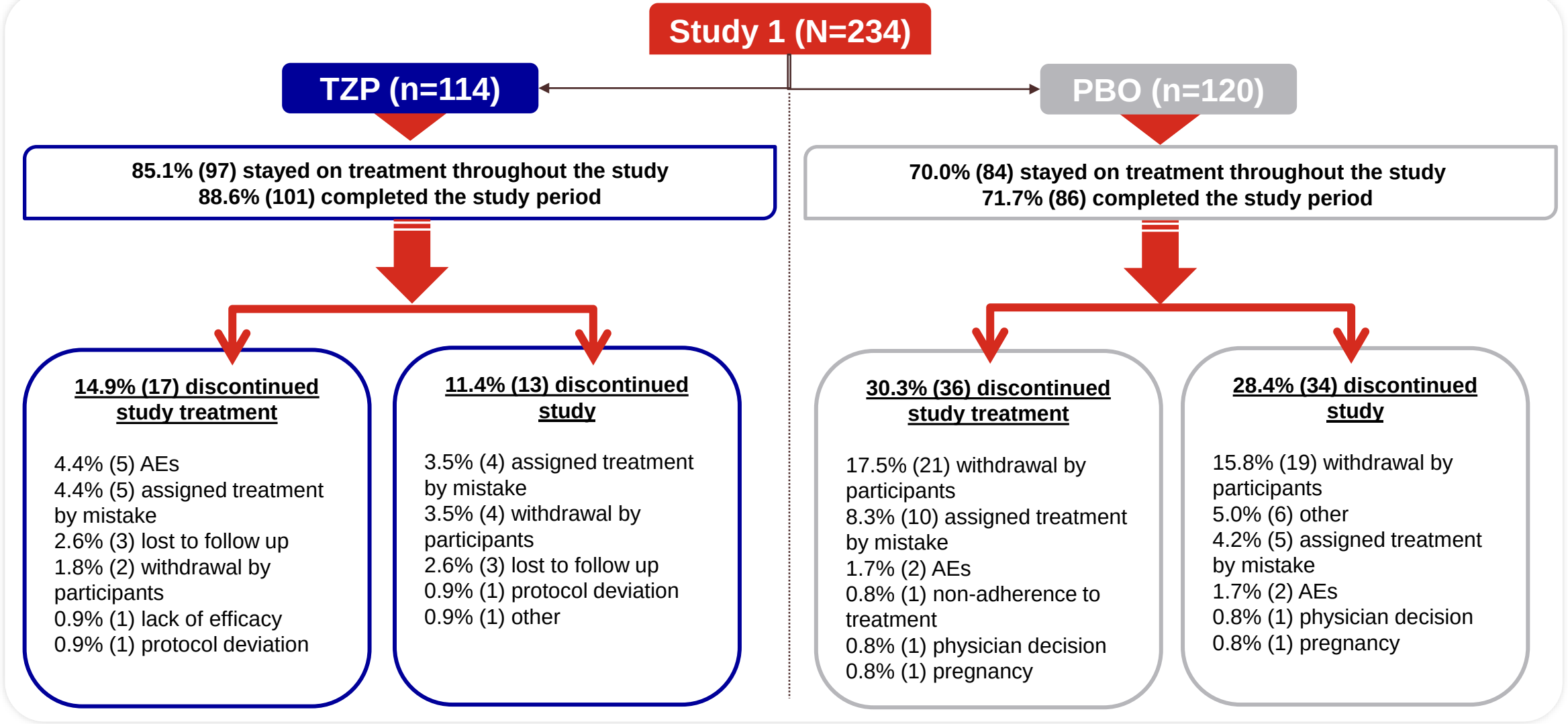


AHI=Apnea-Hypopnea Index; BMI=Body Mass Index; BW=Body Weight; CMS=Centers for Medicare and Medicaid Services; OSA=Obstructive Sleep Apnea; PAP=Positive Airway Pressure; T1DM=Type 1 Diabetes Mellitus; T2DM=Type 2 Diabetes Mellitus.

1. Malhotra A, et al. *Contemp Clin Trials.* 2024;141:107516. 2. Malhotra A, et al. Poster presented at: *APSS 2023*. Poster: 171.

Participant Disposition

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy



AE=Adverse Event; PAP=Positive Airway Pressure; PBO=Placebo; TZP=Tirzepatide.

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

SURMOUNT-OSA Endpoints

Primary Endpoint[1,2]

Change in AHI from baseline to Week 52

Key Secondary Endpoints[1,2]

From baseline to Week 52:

- Percentage change in AHI
- Percentage of participants with clinically meaningful change in AHI[a]
- Percentage of participants with OSA remission or mild nonsymptomatic OSA[b]
- Change in SASHB
- Percentage change in body weight
- Change in inflammatory status (hsCRP)
- Change in PROMIS Short Form Sleep-Related Impairment 8a[c]
- Change in PROMIS Short Form Sleep Disturbance 8b[c]

From baseline to Week 48[d]:

- Change in systolic BP

Graphical Testing Scheme

[a]%Participants with ≥50% reduction in AHI.
[b]Percent of participants with AHI <5 or AHI 5-14 without excessive sleepiness measured by Epworth Sleepiness Scale ≤10.
[c]PROMIS type 1 error-controlled endpoints from both studies were pooled and tested using a distinct graphical testing scheme to provide relevant power for analysis.
[d]BP was assessed at Week 48 because PAP suspension at Week 52 may confound BP measurement.
AHI=Apnea-Hypopnea Index; BP=Blood Pressure; hsCRP=High-Sensitivity C-reactive Protein; OSA=Obstructive Sleep Apnea; PAP=Positive Airway Pressure; PROMIS=Patient-Reported Outcomes Measurement Information System; SASHB=Sleep Apnea Specific Hypoxic Burden.

1. Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print). 2. https://clinicaltrials.gov/study/NCT05412004 (Accessed April 17, 2024).

Baseline Characteristics

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

Parameters	Total (N=234)	TZP (N=114)	PBO (N=120)
Age (years)	47.9±11.5	47.3±11.0	48.4±11.9
<50 years	125 (53.4)	63 (55.3)	62 (51.7)
≥50 years	109 (46.6)	51 (44.7)	58 (48.3)
Female, n (%)	77 (32.9)	36 (31.6)	41 (34.2)
Race/ethnicity, n (%)			
Black or African American	13 (5.6)	6 (5.3)	7 (5.8)
American Indian or Alaska Native	18 (7.7)	9 (7.9)	9 (7.5)
Asian	47 (20.1)	23 (20.2)	24 (20.0)
White	154 (65.8)	74 (64.9)	80 (66.7)
Multiple	2 (0.9)	2 (1.8)	0
Hispanic or Latino	98 (41.9)	51 (44.7)	47 (39.2)
Body Weight, kg	114.7 ± 23.7	116.7 ± 24.6	112.8 ± 22.6
Mean BMI, kg/m^2	39.1 ± 7.0	39.7 ± 7.3	38.6 ± 6.7
BMI category, n (%)[a]			
<35	77 (32.9)	33 (28.9)	44 (36.7)
≥35 to <40	74 (31.6)	39 (34.2)	35 (29.2)
≥40	83 (35.5)	42 (36.8)	41 (34.2)
Waist circumference, cm	121.2 ± 15.7	122.6 ± 16.6	119.8 ± 14.8

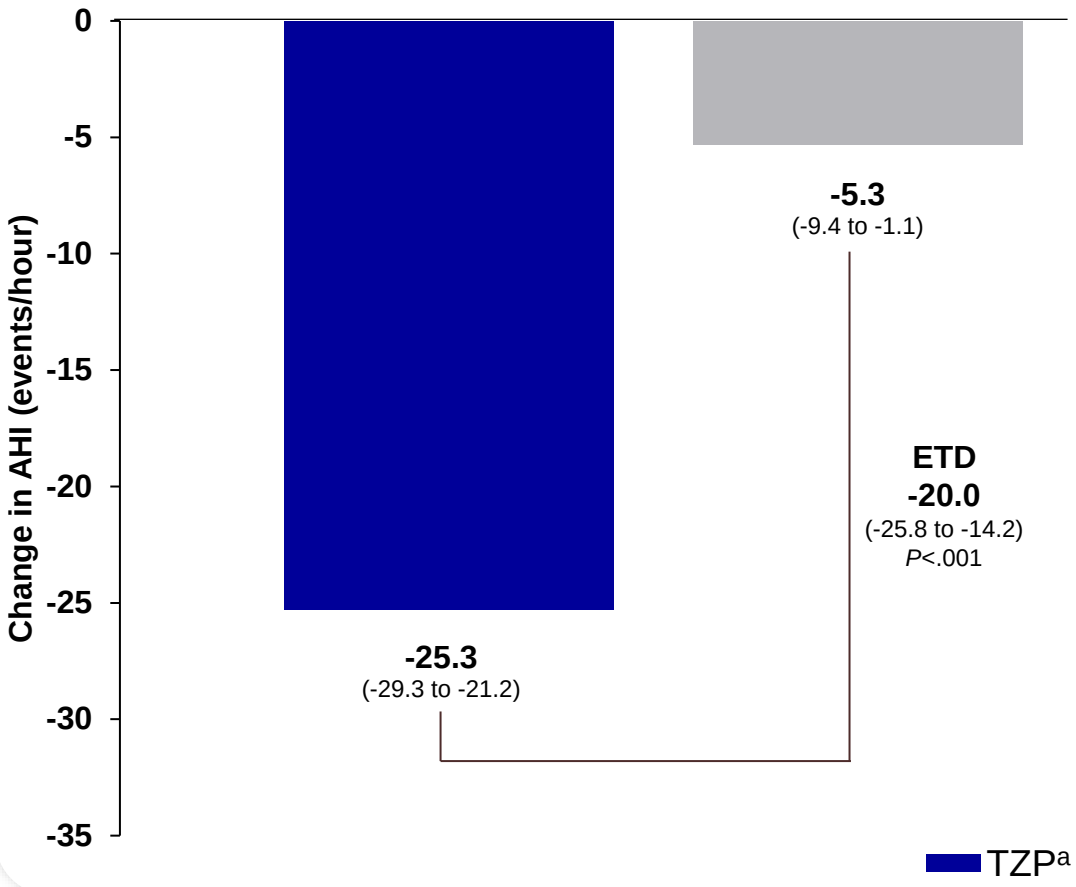
Parameters	Total (N=234)	TZP (N=114)	PBO (N=120)
AHI, events/hour	51.5 ± 31.0	52.9 ± 30.5	50.1 ± 31.5
OSA severity[b], n (%)			
No Apnea	1 (0.4)	0	1 (0.8)
Mild (≥5 to <15 AHI events/hour)	3 (1.3)	1 (0.9)	2 (1.7)
Moderate (≥15 to <30 AHI events/hour)	82 (35.2)	39 (34.2)	43 (36.1)
Severe (≥30 AHI events/hour)	147 (63.1)	74 (64.9)	73 (61.3)
Missing	1	0	1
ESS	10.6 ± 5.3	10.3 ± 5.3	10.8 ± 5.2
SASHB, %min/hour[c]	145.3 (103.4)	153.6 (102.7)	137.8 (104.1)
PROMIS Sleep-Related Impairment T-Score	53.8 ± 8.1	53.2 ± 7.5	54.3 ± 8.5
PROMIS Sleep Disturbance T-Score	53.6 ± 6.7	53.8 ± 6.0	53.5 ± 7.4
Hypertension, n (%)	177 (75.6)	84 (73.7)	93 (77.5)
Systolic BP (mmHg)	129.4 (11.5)	128.4 (12.2)	130.3 (10.7)
Diastolic BP (mmHg)	83.8 (8.7)	83.7 (8.9)	84.0 (8.6)
hsCRP (mg/L)	3.5 (122.0)	3.6 (124.6)	3.5 (120.0)
HbA1c (%)	5.67 ± 0.36	5.69 ± 0.37	5.64 ± 0.35
Prediabetes n (%)	152 (65.0)	74 (64.9)	78 (65.0)
Dyslipidemia n (%)	189 (80.8)	91 (79.8)	98 (81.7)

Note=Data are mean±standard deviation unless otherwise stated.
Footnotes, abbreviations and references are available in speaker notes section.

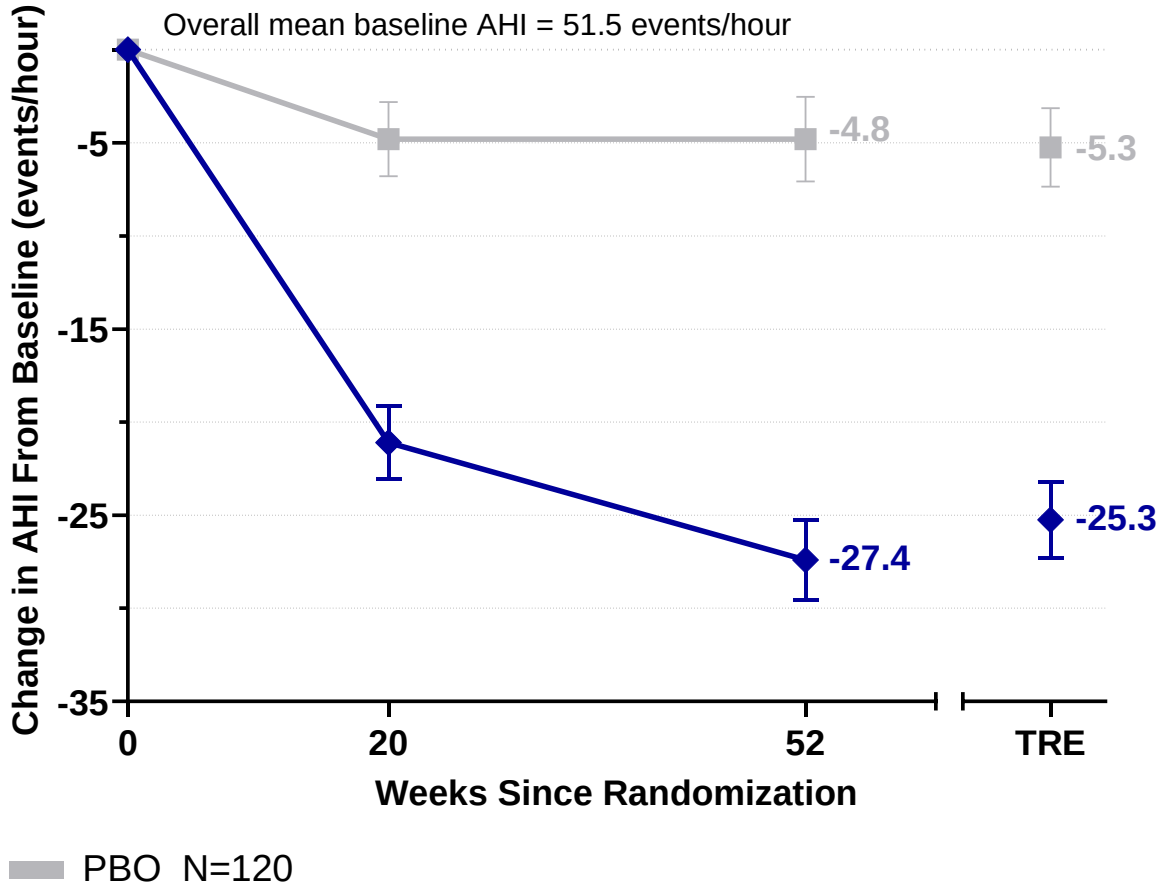
Primary Endpoint - Change in AHI

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

Change From Baseline in AHI at Week 52 (TRE)



Change in AHI by Visit (Efficacy Estimand)



[a]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

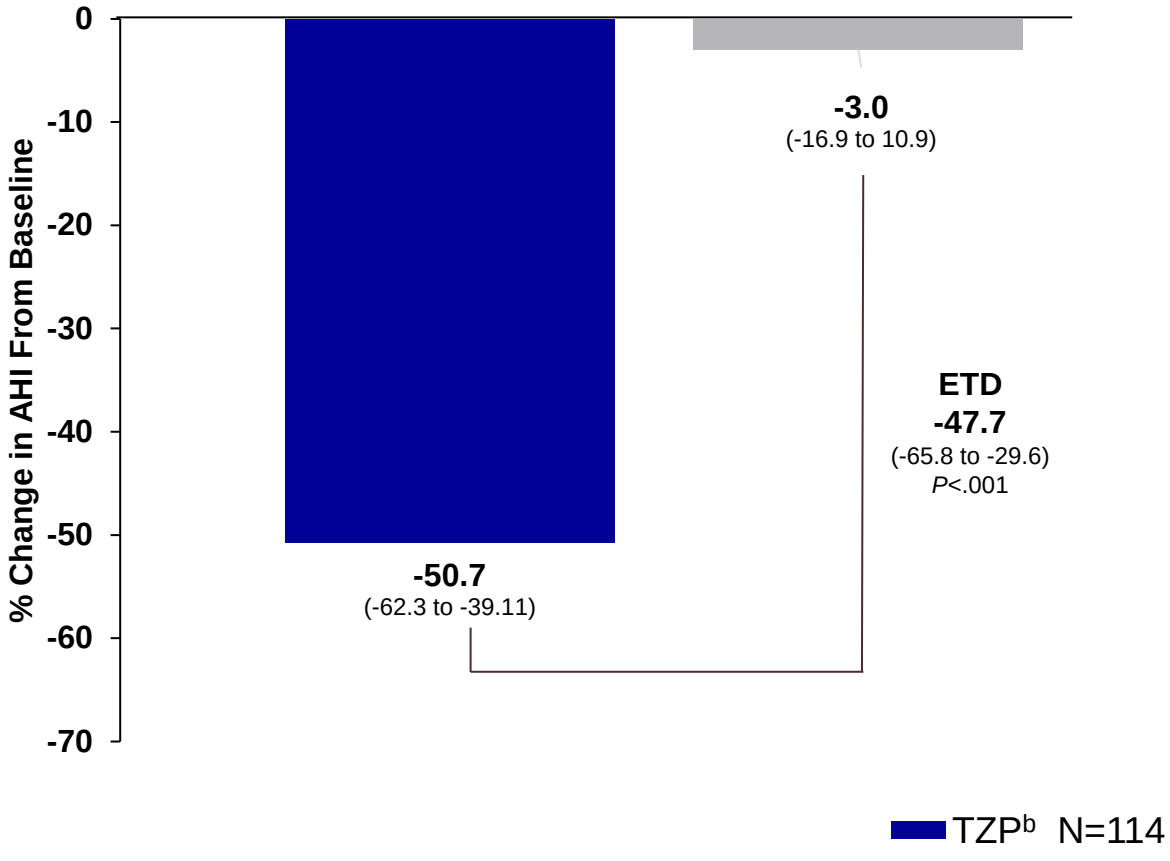
AHI=Apnea-Hypopnea Index; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

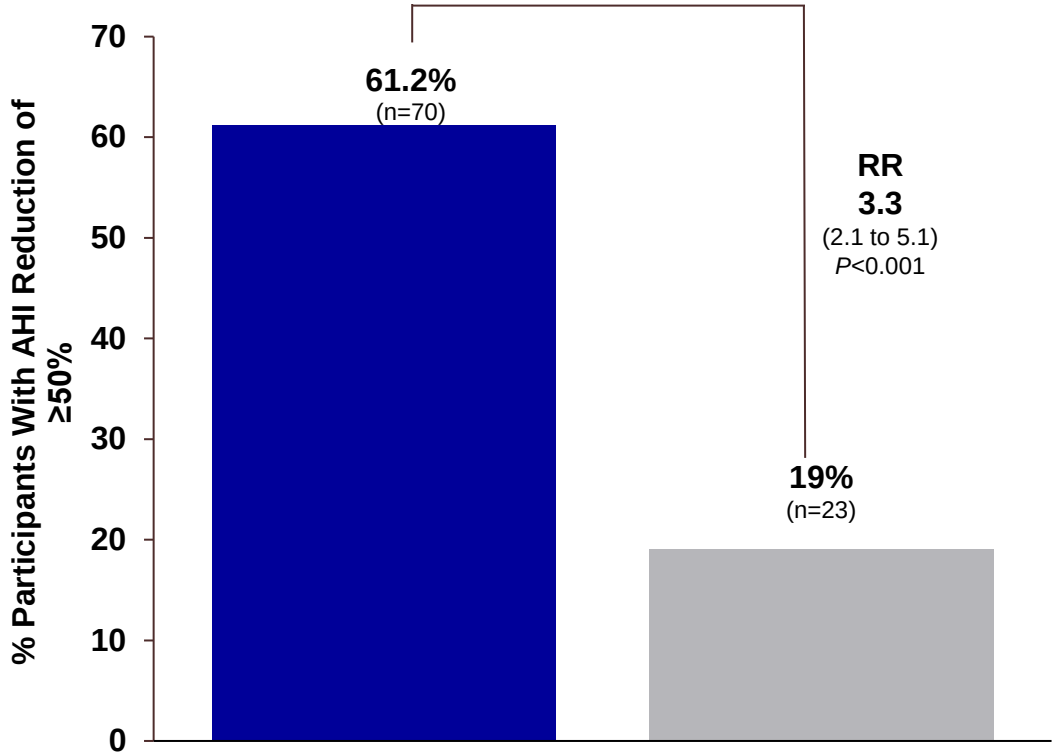
Change in Sleep Disordered Breathing-Related Endpoints

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy (1 of 2)

Percent Change From Baseline in AHI at Week 52 (TRE)



Participants With AHI Reduction of ≥50% at Week 52[a] (TRE)



Percent change in AHI at 52 weeks and participants with AHI reduction of ≥50% at 52 weeks were key secondary endpoints.

[a]Relative risks are calculated using g-computation methods from logistic regression. *P*-values for categorical endpoints are based on logistic regression model.

[b]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

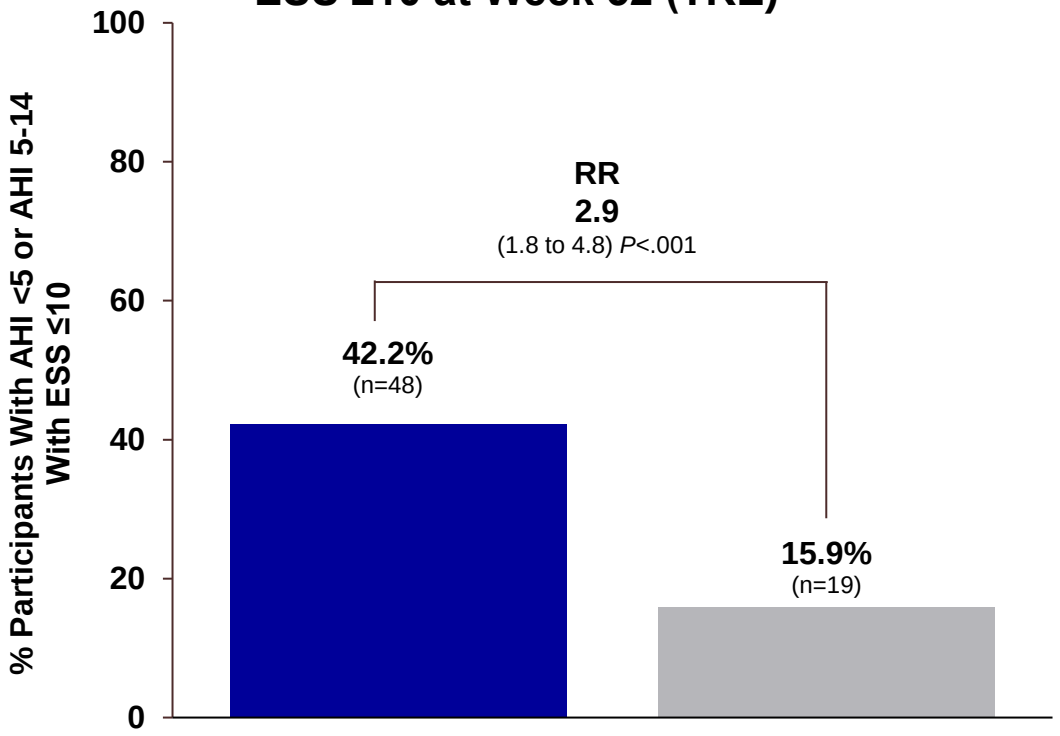
AHI=Apnea-Hypopnea Index; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; RR=Relative Risk; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

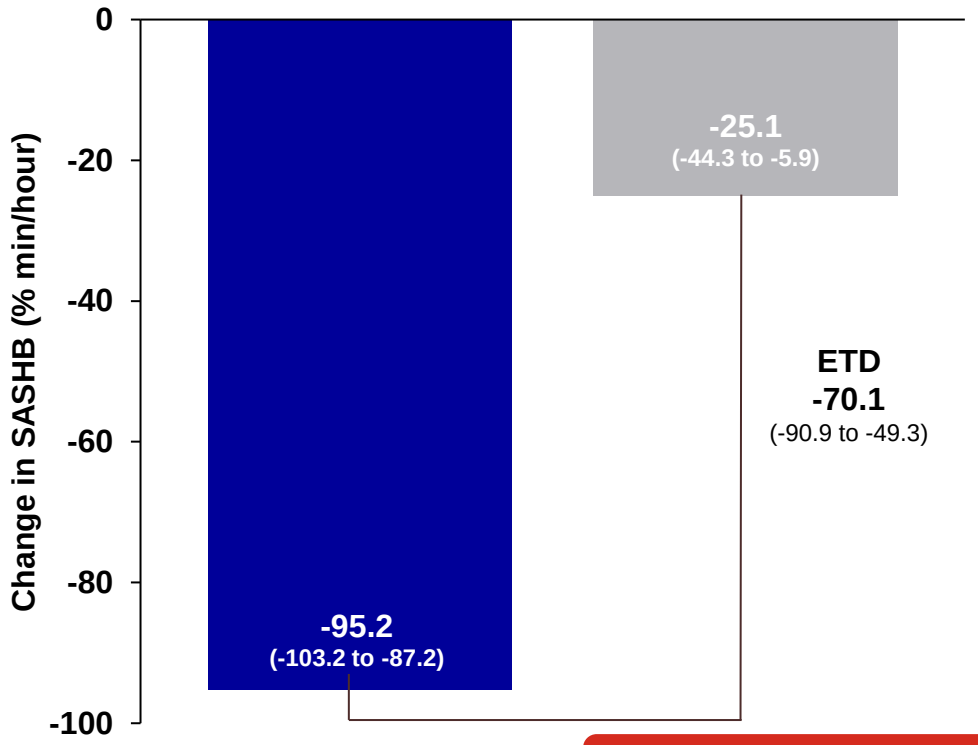
Change in Sleep Disordered Breathing-Related Endpoints

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy (2 of 2)

Participants With AHI <5 or AHI 5-14 With ESS ≤10 at Week 52 (TRE)[a]



Change From Baseline in SASHB at Week 52 (TRE)



TZP[b] N=114 PBO N=120

SASHB

Percent of participants with AHI <5 or AHI 5-14 with ESS ≤10 at Week 52 and change in SASHB at Week 52 were key secondary endpoints.

[a]Relative risks are calculated using g-computation methods from logistic regression. *P*-values for categorical endpoints are based on logistic regression model.

[b]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate 15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

AHI=Apnea-Hypopnea Index; ESS=Epworth Sleepiness Scale; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; RR=Relative Risk; SASHB=Sleep Apnea Specific Hypoxic Burden; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

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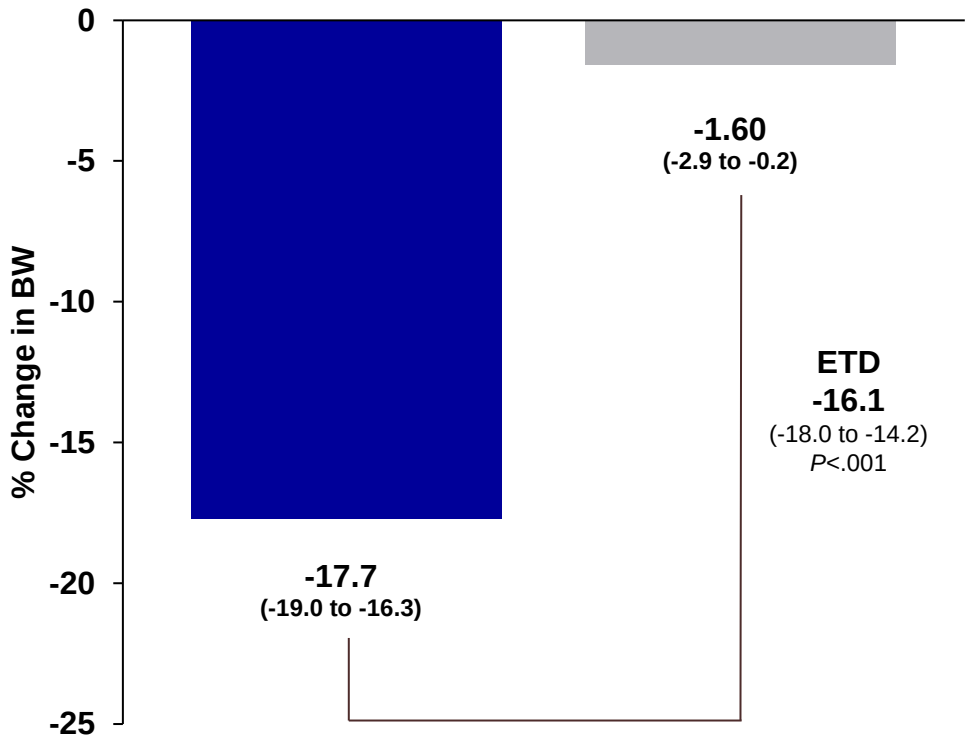
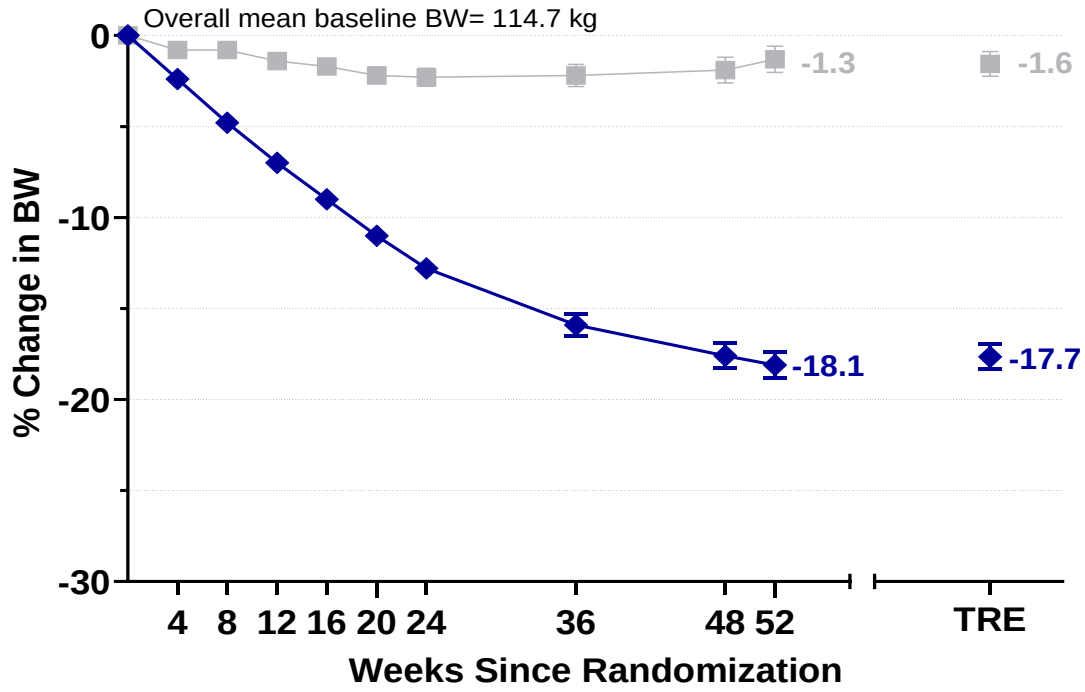
Change in BW

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

Percent Change in BW (TRE)



Percent Change in BW by Visit (Efficacy Estimand)



TZP[a] N=114 PBO N=120

Percent change in BW at Week 52 was a key secondary endpoint.

[a]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

BW=Body Weight; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

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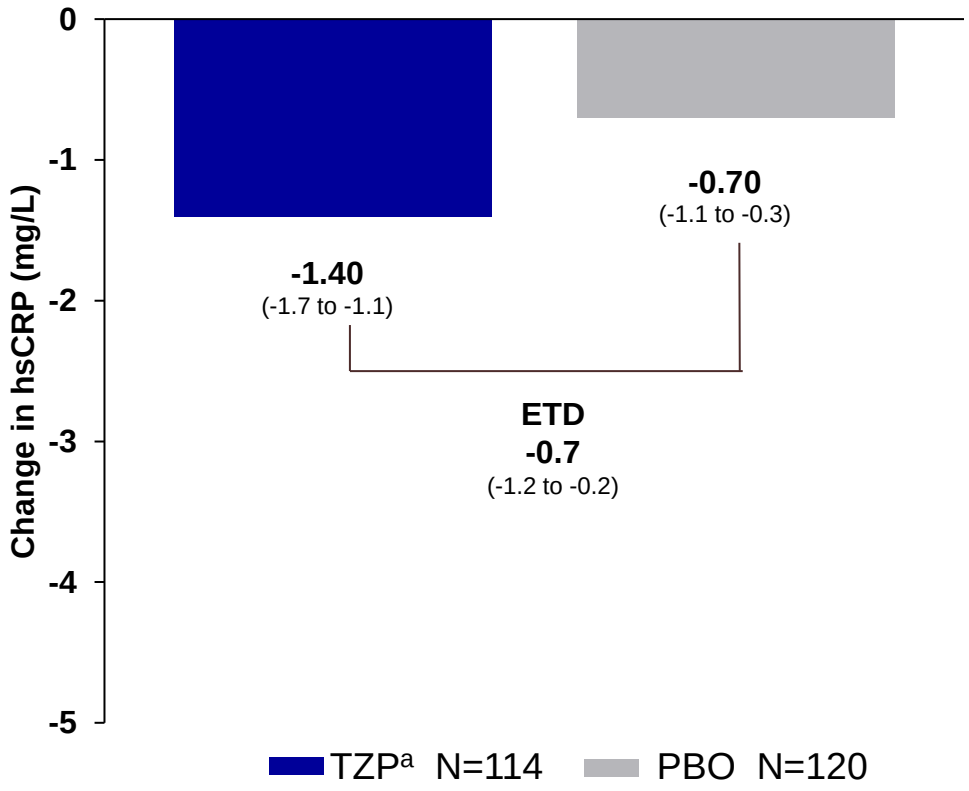
Change in hsCRP

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy



Change in hsCRP was a key secondary endpoint.

[a]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate15 mg continued on 10 mg as their MTD.

Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated. Changes are from baseline to Week 52.

ETD=Estimated Treatment Difference; hsCRP=High-Sensitivity C-reactive Protein; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

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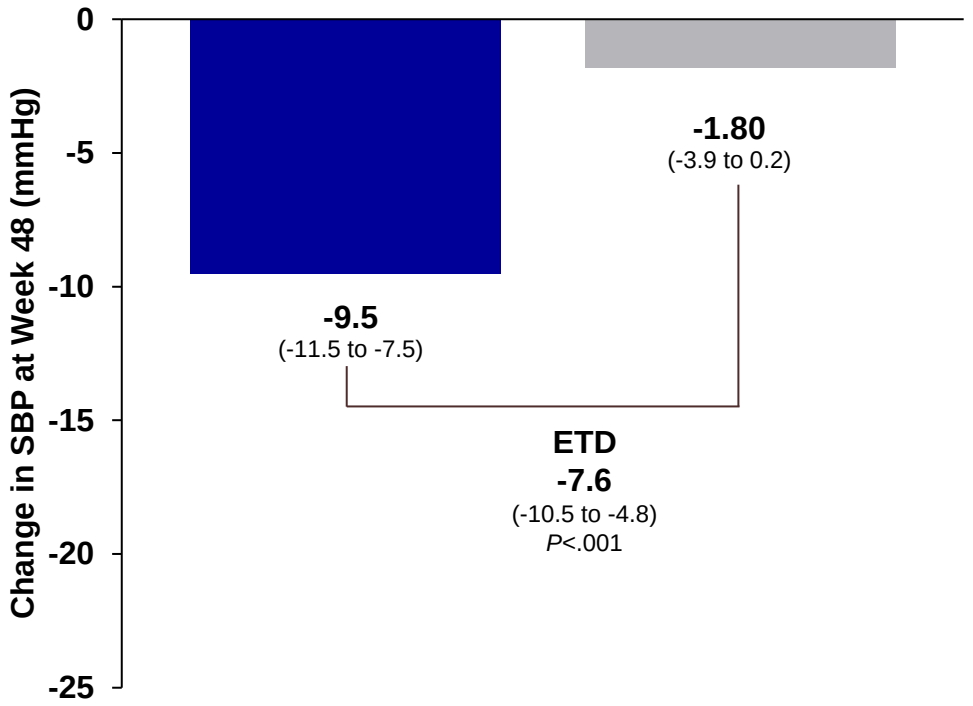
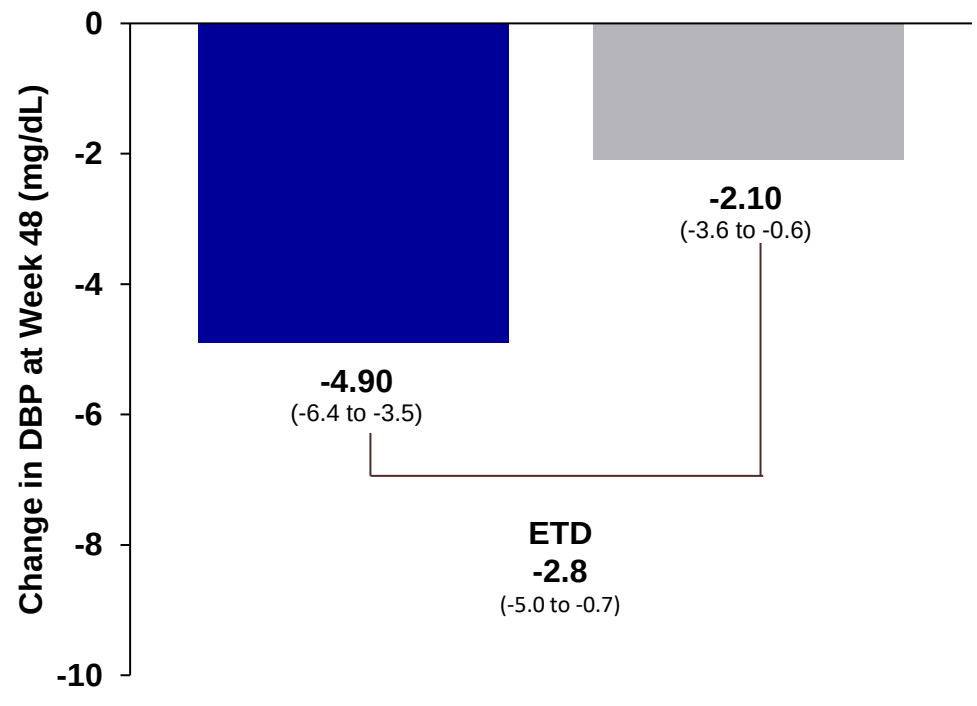
Change in BP at 48 Weeks

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

Change From Baseline in SBP at Week 48[a] (TRE)



Change From Baseline in DBP at Week 48[a,b] (TRE)



TZP[c] N=114 PBO N=120

SBP was a key secondary endpoint and DBP was an additional secondary endpoint.[b]

[a]BP was assessed at Week 48 because PAP suspension at Week 52 may confound BP measurement.

[b]Confidence intervals for any endpoint that is not part of the primary or key secondary endpoints, have not been adjusted for multiplicity and should not be used to make inferences.

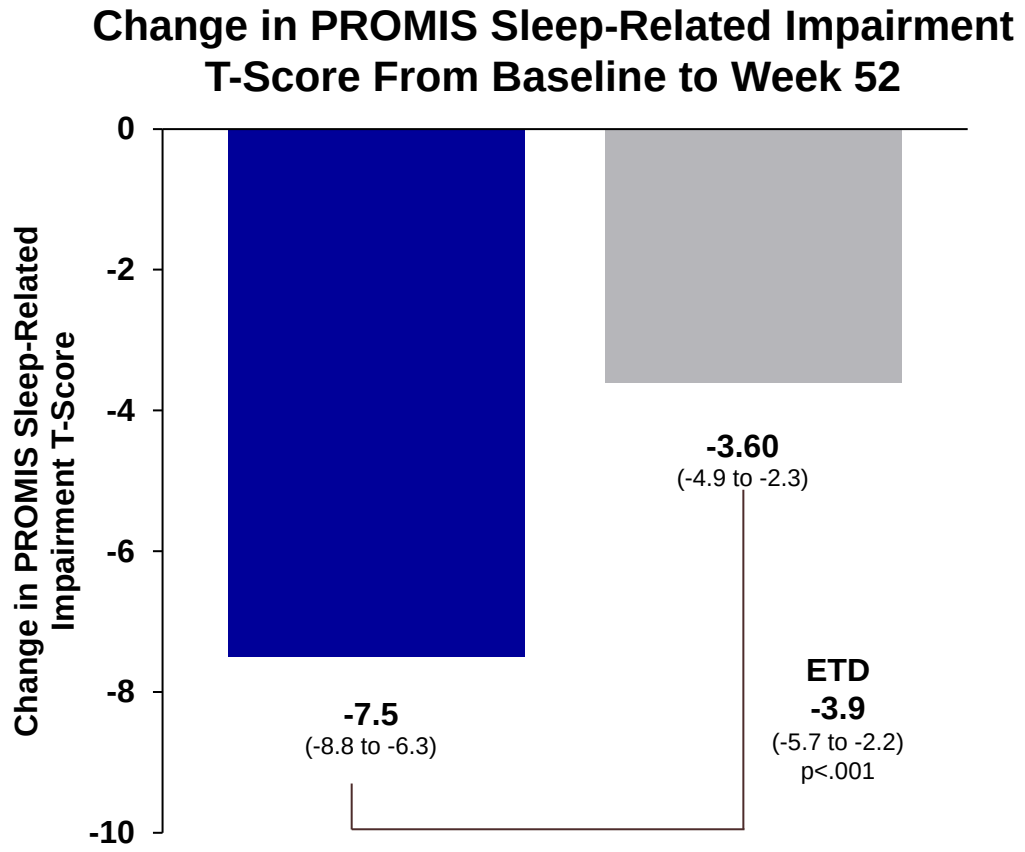
[c]TZP MTD is a maximum tolerated dose of 10 mg or 15 mg once weekly. The starting dose of 2.5 mg TZP was increased by 2.5 mg every 4 weeks until MTD was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but did not tolerate15 mg continued on 10 mg as their MTD.

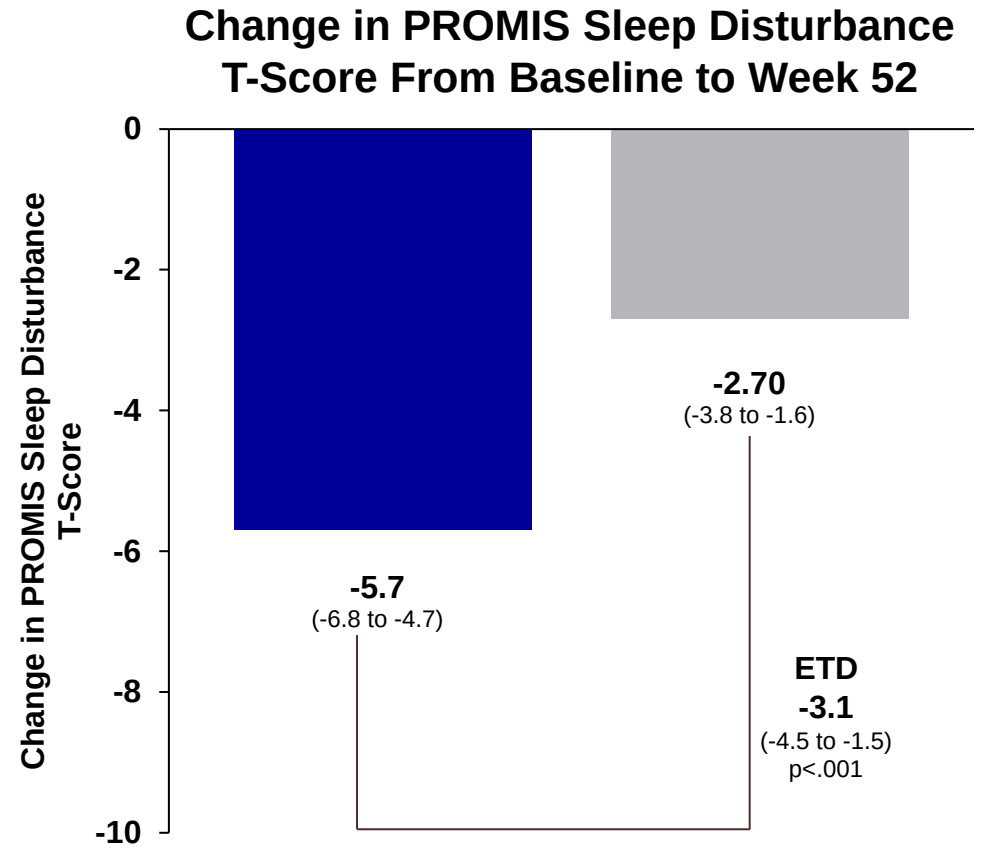
Note: Data are least-squares means (95% confidence interval) or n (%), unless otherwise stated.

BP=Blood Pressure; DBP=Diastolic Blood Pressure; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; SBP=Systolic Blood Pressure; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

Pooled Study 1 and Study 2 Patient-Reported Outcomes





TZP[a] N=234 PBO N=233

Graphical testing scheme

Study 1 PROs

Study 2 PROs

Footnotes, abbreviations and references are available in speaker notes section.
Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

Adverse Events

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

AEs	TZP (N=114) n(%)	PBO (N=120) n(%)
Participants with ≥1 treatment-emergent AEs	91 (79.8)	92 (76.7)
SAEs	9 (7.9)	7 (5.8)
AEs leading to discontinuation of TZP or PBO	5 (4.4)	2 (1.7)
AEs occurring in ≥5% of participants in any treatment group*		
Diarrhea	30 (26.3)	15 (12.5)
Nausea	29 (25.4)	12 (10.0)
Vomiting	20 (17.5)	5 (4.2)
Constipation	18 (15.8)	3 (2.5)
Eructation	9 (7.9)	0 (0.0)
GERD	9 (7.9)	1 (0.8)
Injection site reaction	8 (7.0)	1 (0.8)
Abdominal pain	7 (6.1)	4 (3.3)
URTI	7 (6.1)	10 (8.3)
COVID-19	6 (5.3)	10 (8.3)
Nasopharyngitis	3 (2.6)	8 (6.7)
Dyspepsia	5 (4.4)	2 (1.7)
Gastroenteritis	3 (2.6)	4 (3.3)
Upper Abdominal Pain	4 (3.5)	2 (1.7)
Influenza	4 (3.5)	8 (6.7)
Arthralgia	3 (2.6)	6 (5.0)
Hypertension	1 (0.9)	1 (0.9)

Note: There were no cases of bronchitis and death events reported in Study 1.
AE=Adverse Event; GERD=Gastro-esophageal Reflux Disorder; PAP=Positive Airway Pressure; PBO=Placebo; SAE=Serious Adverse Event; TZP=Tirzepatide; URTI=Upper Respiratory Tract Infection.
Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

Other AEs of Special Interest

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy

AEs of Special Interest	TZP (N=114) n(%)	PBO (N=120) n(%)
Severe hypoglycemia	0 (0.0)	0 (0.0)
Treatment-emergent arrythmias and cardiac conduction disorders	7 (6.1)	9 (7.5)
Severe or serious GI events[a]	4 (3.5)	0 (0.0)
Severe or serious major depressive disorder/suicidal behavior and ideation events	2 (1.8)	1 (0.8)

In Study 1, there were no cases reported of adjudication-confirmed MACE, severe or serious hepatic events, severe or serious acute renal events, adjudication-confirmed acute pancreatitis, C-cell hyperplasia and thyroid malignancies or severe or serious allergic/hypersensitivity reactions including injection-site reactions and antidrug antibody formation.

[a]In Study 1, 2 participants had diarrhea, 1 had gastrooesophageal reflux disease and 1 had nausea.

AE=Adverse Event; GI=Gastrointestinal; MACE=Major Adverse Cardiac Event; PAP=Positive Airway Pressure; PBO=Placebo; TZP=Tirzepatide.

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SURMOUNT-OSA Summary

SURMOUNT-OSA

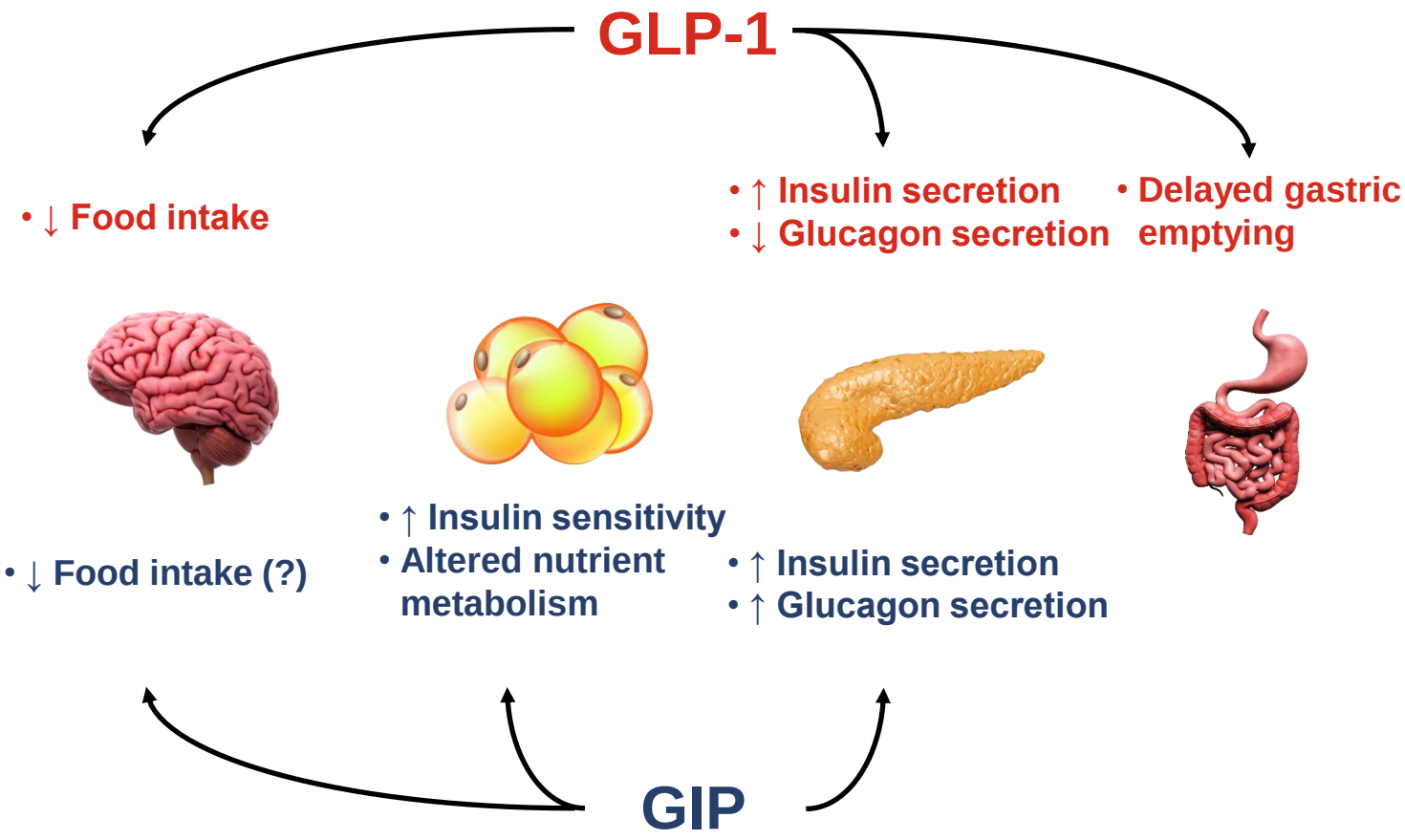
- **SURMOUNT-OSA included two Phase 3 double-blind, randomized, placebo-controlled studies: Study 1 - participants not on PAP therapy; n=234; Study 2 - participants on PAP therapy; n=235**
- **Adults with moderate-to-severe OSA and obesity demonstrated a significant and clinically relevant[a] decrease in AHI with TZP treatment compared to PBO**
- **TZP demonstrated significant improvement in AHI, BW, sleep-related patient-reported outcomes[b], hsCRP, SBP and SASHB in participants with moderate-severe OSA and obesity**
- **The safety and tolerability profile of TZP in participants with moderate-to-severe OSA and obesity was consistent with the safety profile of TZP reported in previous trials**
- **The most frequent adverse events were gastrointestinal-related and were mild to moderate**

[a]According to the AASM, a clinically significant threshold for AHI is defined as ≥15 events/hour.
[b]Includes pooled analysis of PROMIS Sleep-Related Impairment and PROMIS Sleep Disturbance.
AASM=American Academy of Sleep Medicine;AHI=Apnea-Hypopnea Index; BW=Body Weight; hsCRP=High-Sensitivity C-reactive Protein; OSA=Obstructive Sleep Apnea; PAP=Positive Airway Pressure; SASHB=Sleep Apnea Specific Hypoxic Burden; SBP=Systolic Blood Pressure; TZP=Tirzepatide.
Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

Backup

GIP and GLP-1 Receptor Agonist: Potential Mechanism of Action

- GLP-1 has suggested direct actions in the CNS, islets, and stomach[1,2]
- GIP has shown potential actions in research in the CNS (preclinical), adipose tissue (clinical and preclinical), and islets (clinical and preclinical)[2-4]
- A single-molecule GIP/GLP-1 receptor agonist may enable therapeutic actions that are improved over the sum of GIP and GLP-1 single-receptor agonism[5,6]



CNS=Central Nervous System; GIP=Glucose-Dependent Insulinotropic Polypeptide; GLP-1=Glucagon-Like Peptide-1.

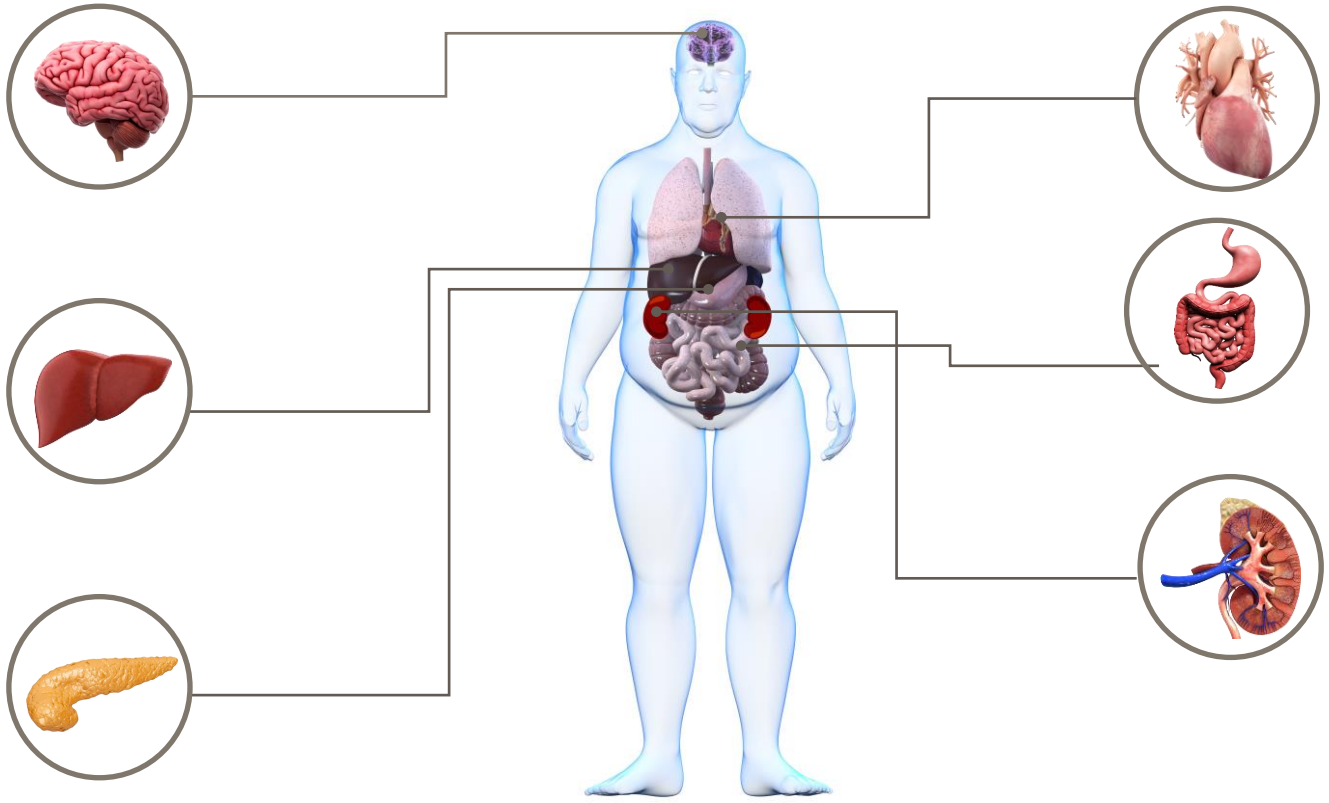
1. Müller TD, et al. *Mol Metab*. 2019;30:72-130. 2. Seino Y, et al. *J Diabetes Investig*. 2010;1(1-2):8-23. 3. Fukuda M. *Diabetes*. 2021;70(8):dbi210001. 4. Nauck MA, et al. *Diabetes Obes Metab*. 2021;23(3):5-29. 5. Samms RJ, et al. *Trends Endocrinol Metab*. 2020;31(6):410-421. 6. Bastin M, et al. *Diabetes Metab Syndr Obes*. 2019;12:1973-1985.

Tirzepatide: Mechanism of Action

CNS
Appetite, feeding behavior

Liver
Liver fat content

Pancreas
Insulin secretion, glucagon regulation



Cardiovascular
Lipid regulation

GI tract
Delayed gastric emptying

Kidney
Proteinuria and renal function

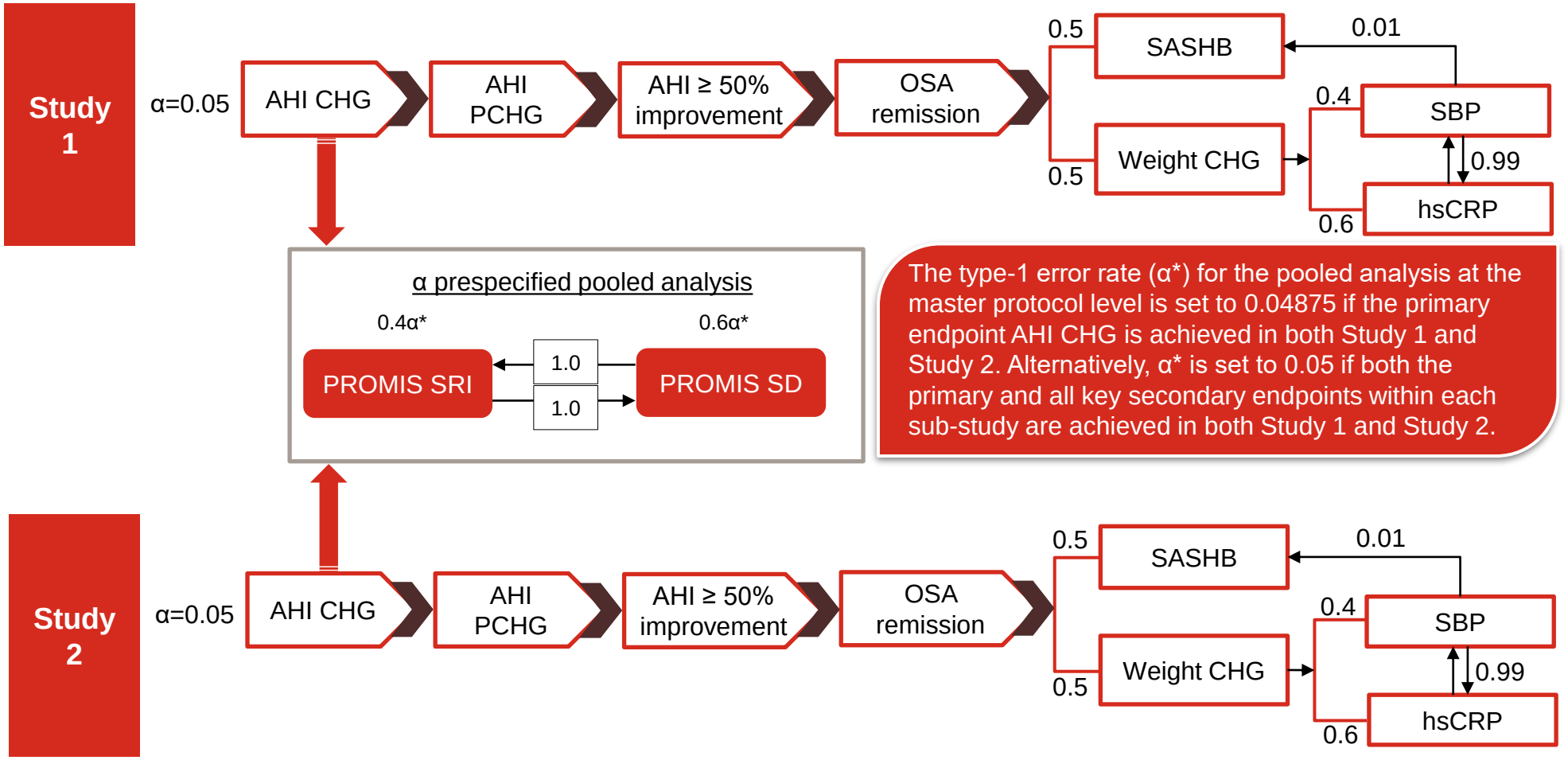
Systemic Effects
Insulin sensitivity

CNS=Central Nervous System; GI=Gastrointestinal.

1. Heise T, et al. Oral presentation at: *ADA 2022*. Abstract 338-OR. 2. Heise T, et al. *Lancet Diabetes Endocrinol*. 2022;10(6):418-429. 3. Gastaldelli A, et al. *Lancet Diabetes Endocrinol*. 2022;10(6):393-406. 4. Samms RJ, et al. *Trends Endocrinol Metab*. 2020;31(6):410-421. 5. Patel H, et. al. Oral presentation at: 58th EASD. Abstract 568.

SURMOUNT-OSA Endpoints

Pre-specified Multiplicity Control for SURMOUNT-OSA Master Protocol



The type-1 error rate (α*) for the pooled analysis at the master protocol level is set to 0.04875 if the primary endpoint AHI CHG is achieved in both Study 1 and Study 2. Alternatively, α* is set to 0.05 if both the primary and all key secondary endpoints within each sub-study are achieved in both Study 1 and Study 2.

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

[a]%Parti
[b]Percer
[c]PROM
[d]BP wa
AHI=Ap
Airway Pr

1. Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print). 2. https://clinicaltrials.gov/study/NCT05412004 (Accessed April 17, 2024).

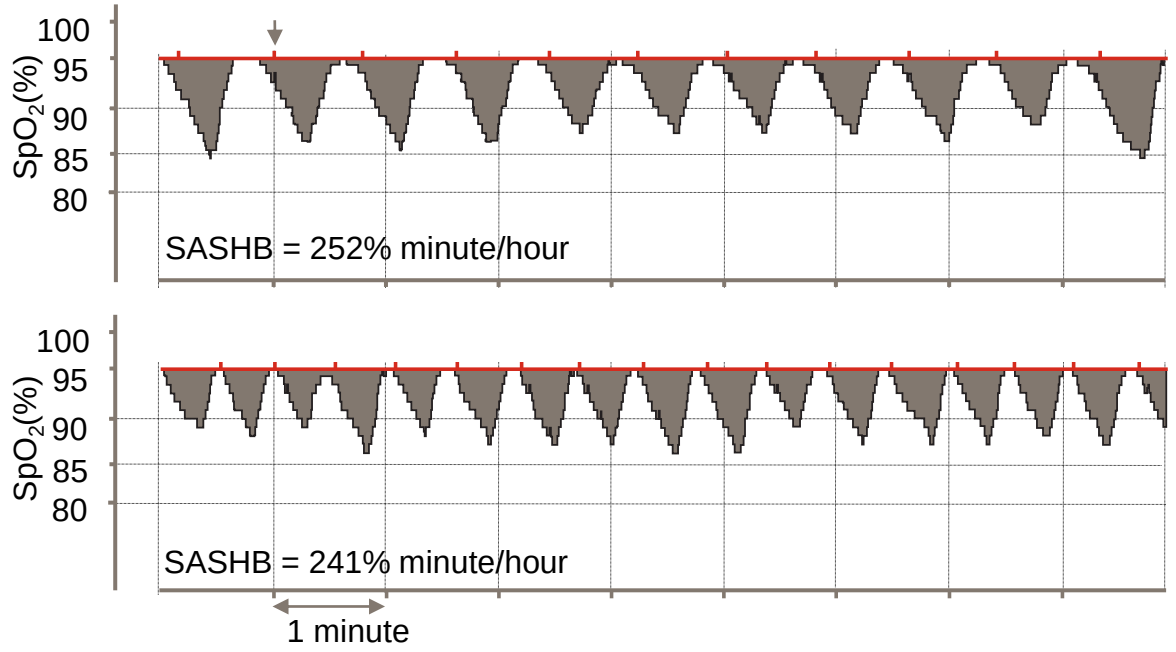
Change in Sleep Disordered Breathing-Related Endpoints

SURMOUNT-OSA Study 1: Participants Not on PAP Therapy (2 of 2)

Sleep Apnea-Specific Hypoxic Burden (SASHB)

- Area under the curve below the pre-event SpO_2 baseline
- Expressed as %minutes/hour

  (SASHB of 50%min/h = 5% reduction in SpO_2 below baseline for 10 min every hour of sleep)



Cardiovascular outcomes are more strongly and consistently (across cohorts) associated with a quantitative measure of SASHB than the usual measure of respiratory event frequency (AHI)

Azarbarzin A, et al. *Chest.* 2020;158(2):739-750.

AHI=Apnea-Hypopnea Index; ESS=Epworth Sleepiness Scale; ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; RR=Relative Risk; SASHB=Sleep Apnea Specific Hypoxic Burden; TRE=Treatment-Regimen Estimand; TZP=Tirzepatide.

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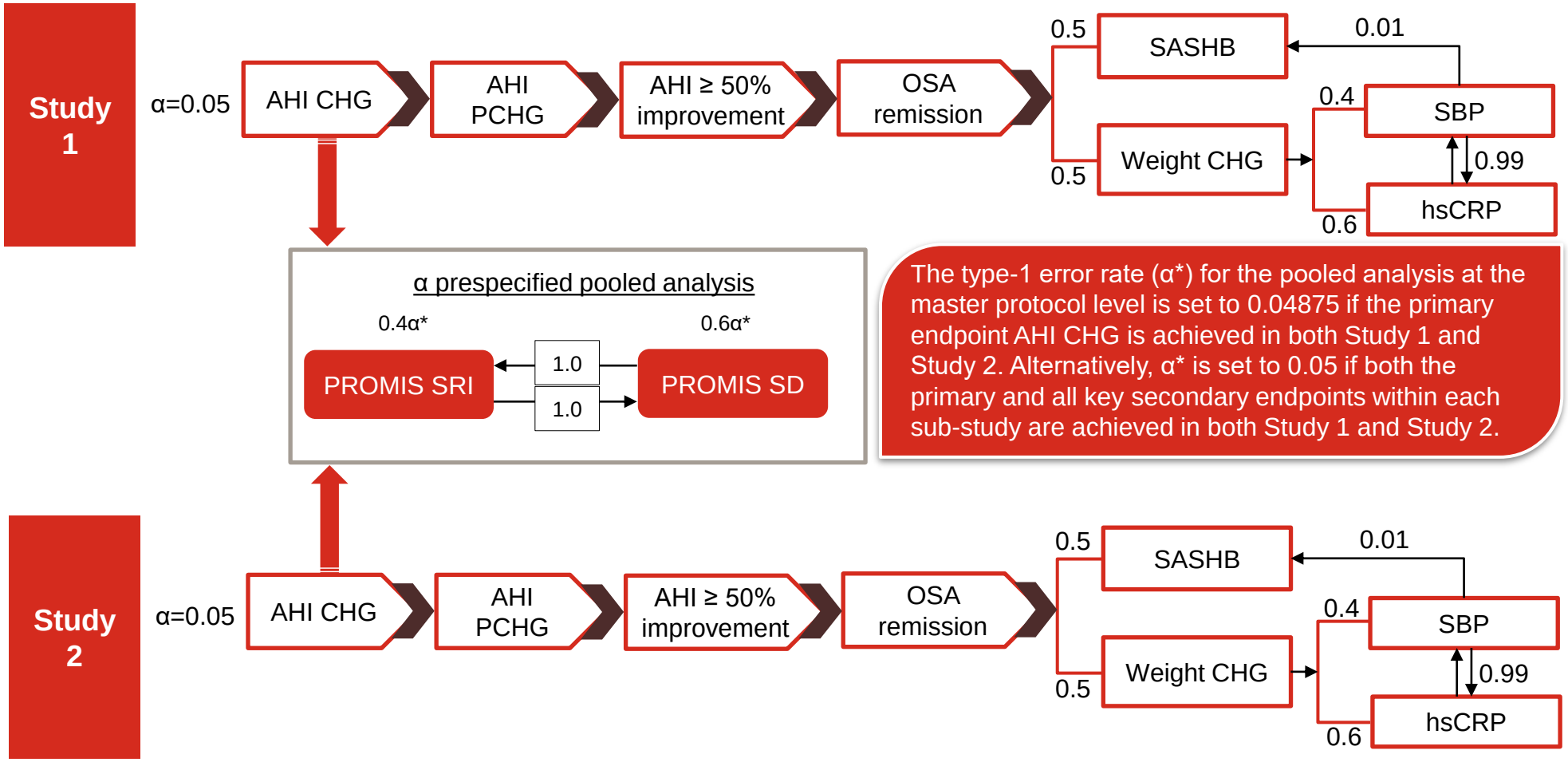
Pre-specified Multiplicity Control for SURMOUNT-OSA Master Protocol



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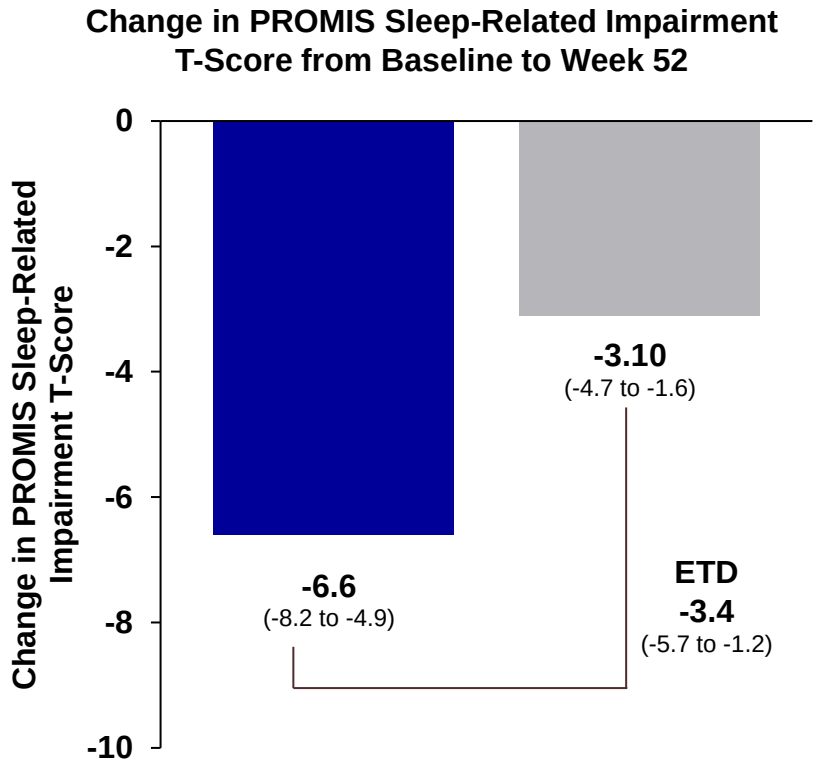
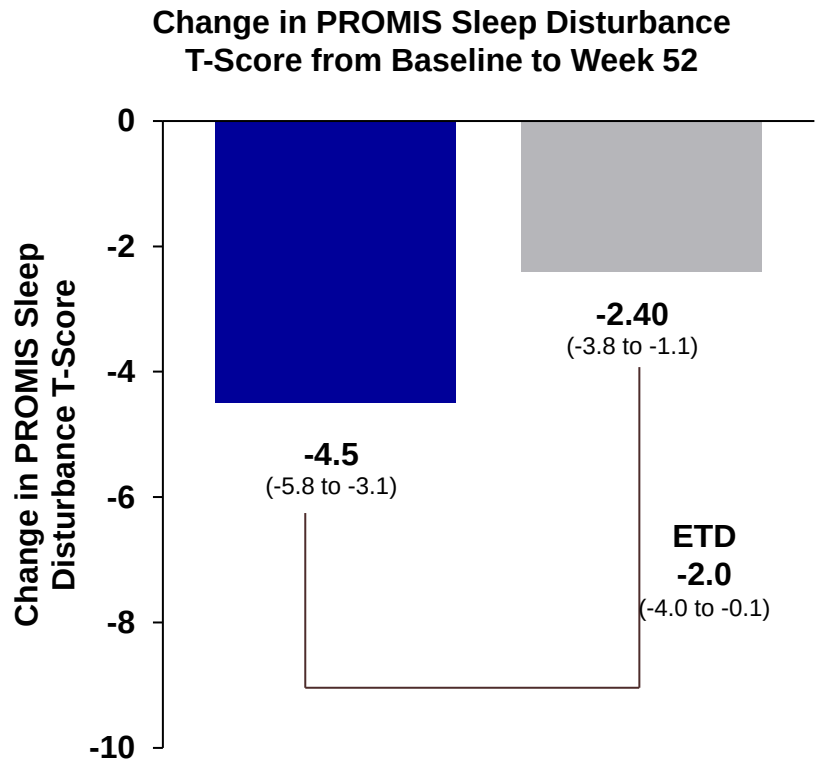
Pooled Study 1 and Study 2 Patient-Reported Outcomes

Study 1 Patient-Reported Outcomes





TZP N=114 PBO N=120

Malhotra A, et al. *NEJM*. 2024;doi:10.1056/NEJMoa2404881 (Ahead of Print).

Footnotes, abbreviations and references are available in speaker notes section.
ETD=Estimated Treatment Difference; MTD=Maximum Tolerated Dose; PAP=Positive Airway Pressure; PBO=Placebo; PROMIS=Patient-Reported Outcomes Measurement Information System; TZP=Tirzepatide.
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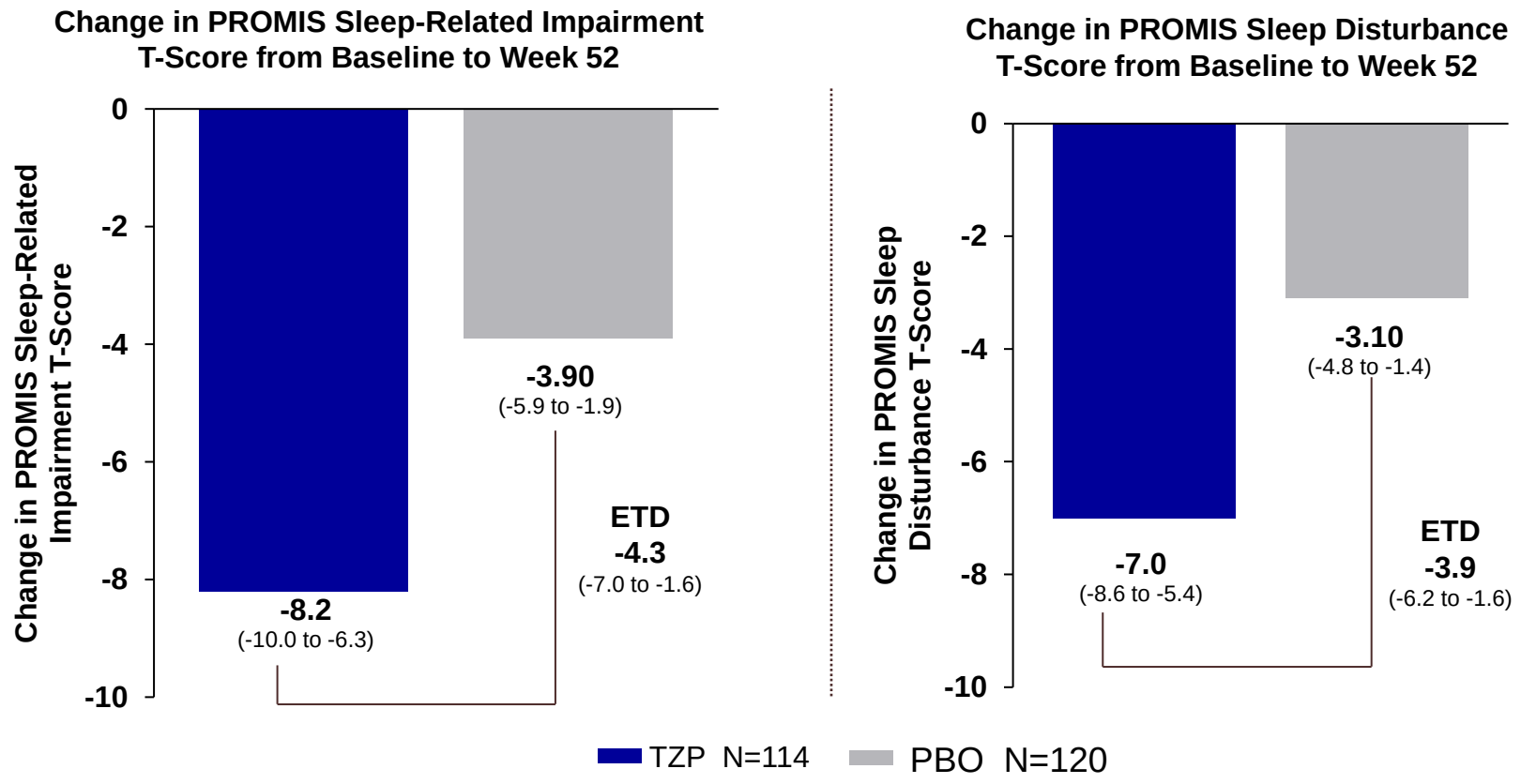
Pooled Study 1 and Study 2 Patient-Reported Outcomes

Study 2 Patient-Reported Outcomes



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