Waist-to-Height Ratio Shifts Over Time in Tirzepatide-Treated Participants – Post Hoc Analysis in SURMOUNT-1 and SURMOUNT-2

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OBJECTIVE

- To assess change from baseline to Week 72 in WHtR and shift from baseline to Week 72 in WHtR central adiposity categories as defined by UK NICE[1] guidelines for individuals with BMI <35 kg/m^2:
  - **Healthy**: WHtR 0.4 - 0.49, indicating no increased health risk
  - **Increased**: WHtR 0.5 – 0.59, indicating increased health risks
  - **High**: WHtR 0.6 or more, indicating further increased health risks

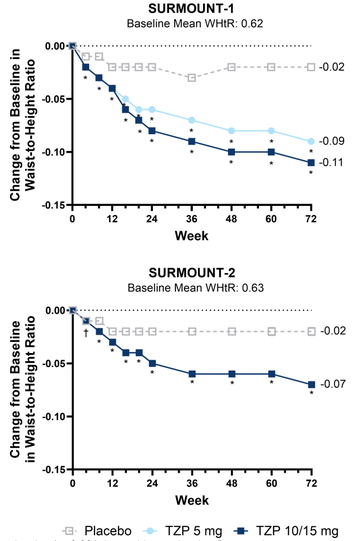
CONCLUSION

- In this post hoc analysis, treatment with tirzepatide in participants with BMI <35 kg/m^2 was associated with:
  - Significant reduction of WHtR
  - Shift to lower WHtR risk categories, with more individuals in "healthy," fewer in "high," and more moving from "high" to "increased" categories.
- In this post hoc analysis, treatment with tirzepatide in participants with BMI ≥35 kg/m^2 was associated with:
  - Similar magnitudes of WHtR reduction as seen in participants with BMI <35 kg/m^2; however, shifts to the healthy WHtR risk category was minimal.
- Future studies could further elucidate the effect of tirzepatide on other cardiometabolic parameters and outcomes and examine how changes in WHtR may explain any such benefits.

American Association of Clinical Endocrinology – 33rd Annual Meeting (AACE); New Orleans, LA; May 9th-11th, 2024

KEY RESULTS

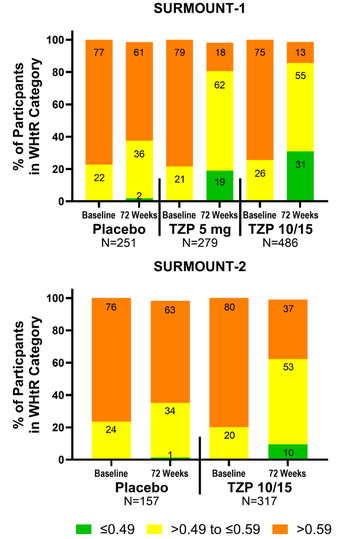
Treatment with tirzepatide was associated with a significant reduction of WHtR compared to placebo at week 72 in participants with BMI <35 kg/m^2



†p=0.04 tirzepatide vs. placebo. *p<0.001 tirzepatide vs. placebo; Data are least square means change from baseline. TZP = tirzepatide

KEY RESULTS

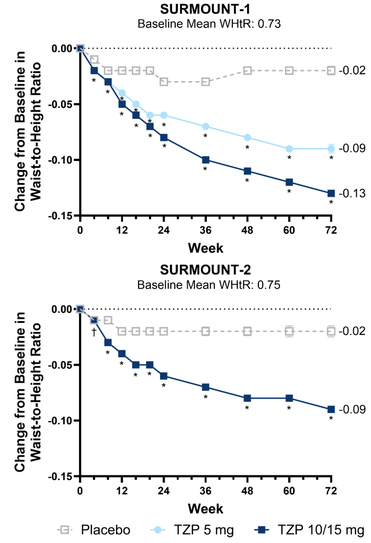
Treatment with tirzepatide was associated with shifts in WHtR risk categories from baseline to week 72 in participants with BMI <35 kg/m^2



There were 16 missing postbaseline values for SURMOUNT-1 and 6 for SURMOUNT-2. N= number of participants, TZP = tirzepatide.

KEY RESULTS

Treatment with tirzepatide was associated with a significant reduction of WHtR compared to placebo at week 72 in participants with BMI ≥35 kg/m^2



†p=0.04 tirzepatide vs. placebo. *p<0.001 tirzepatide vs. placebo; Data are least square means change from baseline. TZP = tirzepatide

Background

- Waist-to-height ratio (WHtR) is a practical estimate of central adiposity and can be a better predictor of cardiometabolic disease than body mass index (BMI).
- Tirzepatide led to significant weight reduction and improved cardiometabolic parameters in SURMOUNT-1 and SURMOUNT-2.[2-3]

Methods

- Post hoc analyses included participants with baseline BMI <35kg/m^2:
  - 1,016 participants in SURMOUNT-1
  - 474 participants in SURMOUNT-2
- Analyses used efficacy analysis sets (on-treatment data in participants with ≥ 1 dose of study drug) and the last non-missing value for WHtR.
- Changes from baseline to Week 72 in WHtR were compared between tirzepatide 5 mg, pooled tirzepatide 10/15 mg, and placebo using mixed model for repeated measures.
- Proportion of participants reaching WHtR category thresholds were also evaluated.

Study Design

SURMOUNT-1

Tirzepatide 5 mg
Tirzepatide 10 mg
Tirzepatide 15 mg
Placebo

Obesity Management
Duration: 72 weeks

Key Inclusion Criteria
- Adults (≥18 years) with BMI ≥30 kg/m^2, or BMI ≥27 kg/m^2 with ≥ 1 weight-related comorbidities

Key Exclusion Criteria
- Type 1 or 2 diabetes
- >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

SURMOUNT-2

Tirzepatide 10 mg
Tirzepatide 15 mg
Placebo

Obesity Management with Type 2 Diabetes
Duration: 72 weeks

Key Inclusion Criteria
- Adults (≥18 years) with BMI ≥27 kg/m^2 with type 2 diabetes who had an HbA1c of 7-10% on stable therapy for at least 3 months before screening

Key Exclusion Criteria
- Type 1 diabetes
- >5 kg body weight change within 90 days before screening
- Prior or planned surgical treatment for obesity
- Treatment with anti-obesity medications, DDP-4 inhibitors, GLP-1 receptor agonist, or any injectable therapy for type 2 diabetes within 3 months of screening

Baseline Characteristics

	SURMOUNT-1		SURMOUNT-2	
Baseline Characteristic	**WHtR ≤0.59[a] (N=241)**	**WHtR >0.59 (N=775)**	**WHtR ≤0.59 (N=101)**	**WHtR >0.59 (N=373)**
Sex, female (%)	151 (62.7)	509 (65.7)	26 (25.7)	186 (49.9)***
Age, years	43.9 (12.3)	47.6 (12.5)***	53.8 (10.4)	55.7 (9.9)*
Height, cm	167.8 (8.7)	165.2 (9.2)***	172.8 (9.1)	166.2 (9.5)***
Body weight, kg	87.0 (10.3)	88.9 (11.1)*	87.4 (10.2)	87.8 (12.3)
BMI, kg/m^2	30.8 (2.1)	32.5 (1.6)***	29.2 (1.9)	31.7 (2.1)***
Waist circumference, cm	94.3 (6.3)	106.2 (7.5)***	97.3 (6.0)	108.5 (7.6)***
HbA_{1c},%	5.4 (0.3)	5.5 (0.4)***	8.0 (0.9)	8.0 (0.9)
Prediabetes, n (%)	66 (27.4)	292 (37.7)**	--	--
Obesity duration, years	10.3 (9.7)	12.4 (10.3)**	13.5 (10.9)	16.3 (11.0)*
Diabetes duration, years	--	--	9.3 (6.3)	9.0 (6.2)
Triglycerides, mg/dL	136.8 (79.4)	157.0 (144.2)*	194.8 (168.2)	183.8 (142.7)
HDL, mg/dL	52.4 (14.4)	50.0 (13.5)*	44.4 (11.1)	44.9 (12.4)
Mean WHtR	0.56 (0.0)	0.64 (0.0)***	0.56 (0.0)	0.65 (0.0)***

Data are mean (standard deviation) for continuous data unless otherwise noted. [a]Included 2 participants with WHtR ≤0.49 at baseline. *p<0.05, **p<0.01 and ***p<0.001 between baseline groups. BMI = body mass index; HbA_{1c} = glycated hemoglobin; WHtR = waist to height ratio.

References: [1]NICE (2023) *Obesity: identification, assessment and management.* CG189. [2]Jastreboff AM, et al. NEJM 2022;387(3):205-216. [3]Garvey WT, et al. Lancet 2023;402:613-26.

ClinicalTrial.gov Identifiers NCT04184622, NCT04657003. **Disclosures:** BT is an advisor to Novo Nordisk and Palatin Technologies. NS has consulted for and/or received speaker honoraria from Abbott Laboratories, AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Hanmi Pharmaceuticals, Janssen, Menarini-Ricerche, Novartis, Novo Nordisk, Pfizer, Roche Diagnostics, and Sanofi; and received grant support paid to his University from AstraZeneca, Boehringer Ingelheim, Novartis, and Roche Diagnostics. HW is an employee of TechData Services and contracted with Eli Lilly and Company to provide statistical analysis. JPD, XMZ, LEGP, CJM, and JFB are employees and shareholders of Eli Lilly and Company

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BACKGROUND AND OBJECTIVES

Background

- Waist-to-height ratio (WHtR) can be a practical estimate of central adiposity and can be a better predictor of cardiometabolic disease than body mass index (BMI).[1]
- Tirzepatide led to significant weight reduction and improved cardiometabolic parameters in SURMOUNT-1 and SURMOUNT-2.[2-3]

Objective

- The objectives of this post hoc analysis of SURMOUNT-1 and SURMOUNT-2 were to assess:
  - Change from baseline to Week 72 in WHtR
  - Shift from baseline to Week 72 in WHtR central adiposity categories as defined by UK National Institute for Health and Care Excellence[1] (NICE) guidelines for individuals with BMI <35 kg/m^2:
    - **Healthy**: WHtR 0.4 - 0.49, indicating no increased health risks
    - **Increased**: WHtR 0.5 - 0.59, indicating increased health risks
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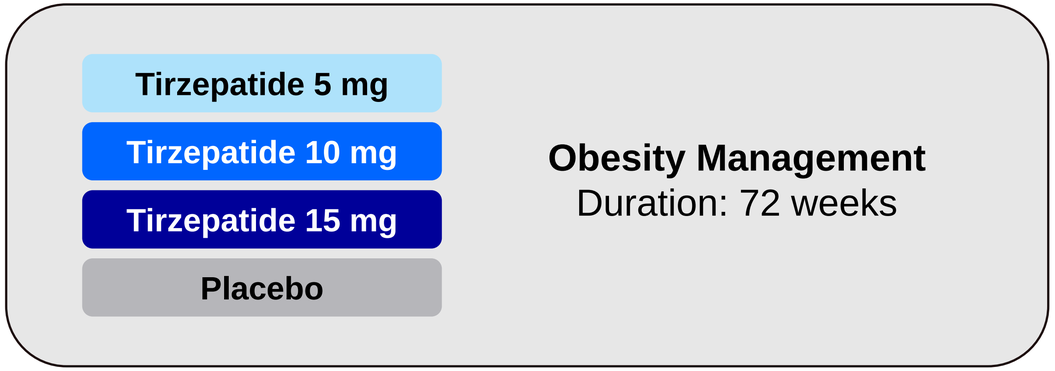
STUDY DESIGN

SURMOUNT-1



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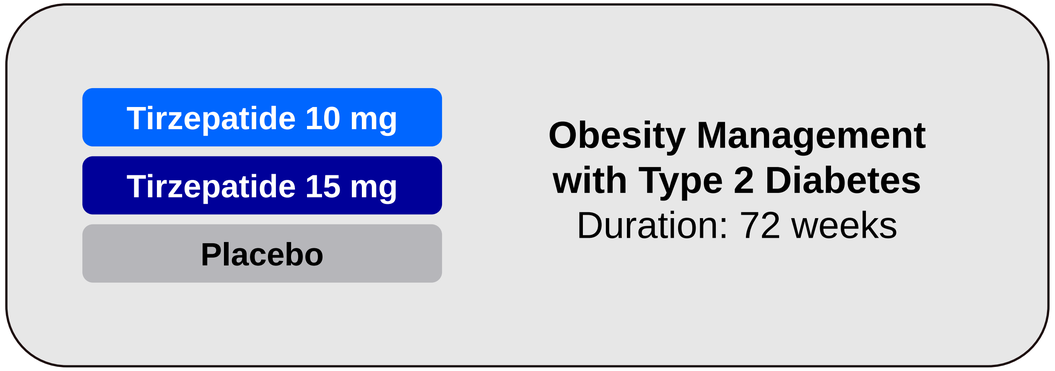
SURMOUNT-2



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METHODS

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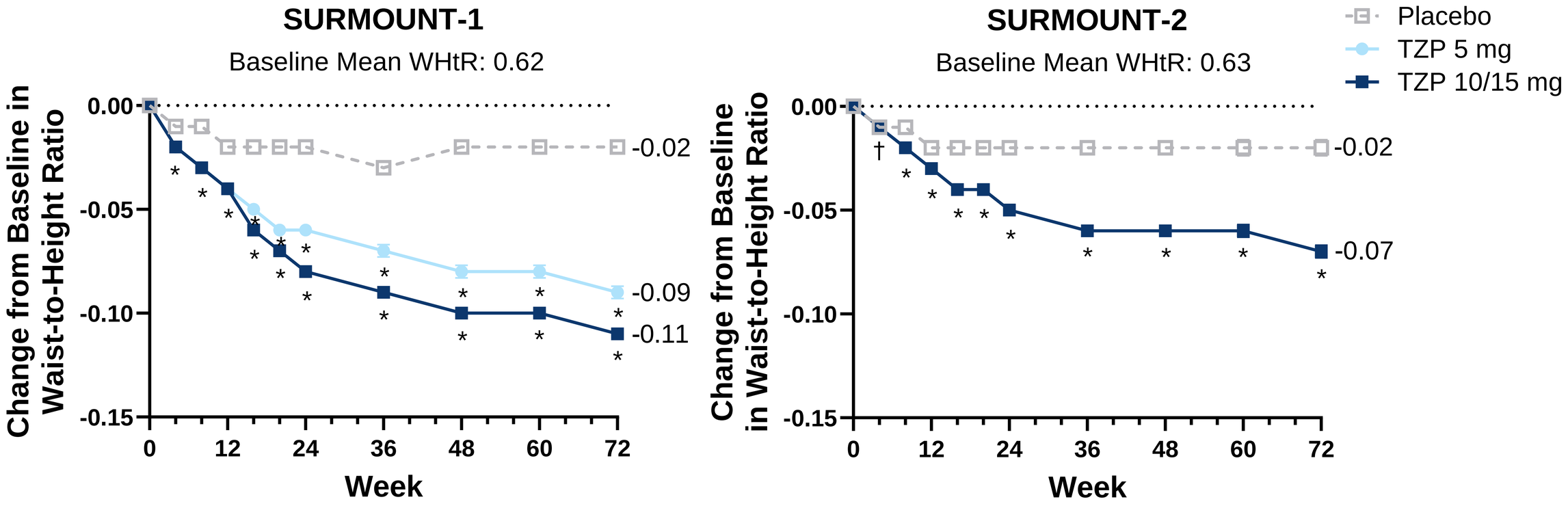
BMI = body mass index; DBP = diastolic blood pressure; HbA_{1c} = glycated hemoglobin; SBP = systolic blood pressure; WHtR = waist to height ratio.

Change from Baseline to Week 72 in WHtR Over Time in Participants with BMI <35 kg/m^2

- Treatment with tirzepatide was associated with a significant reduction of WHtR compared to placebo at Week 72



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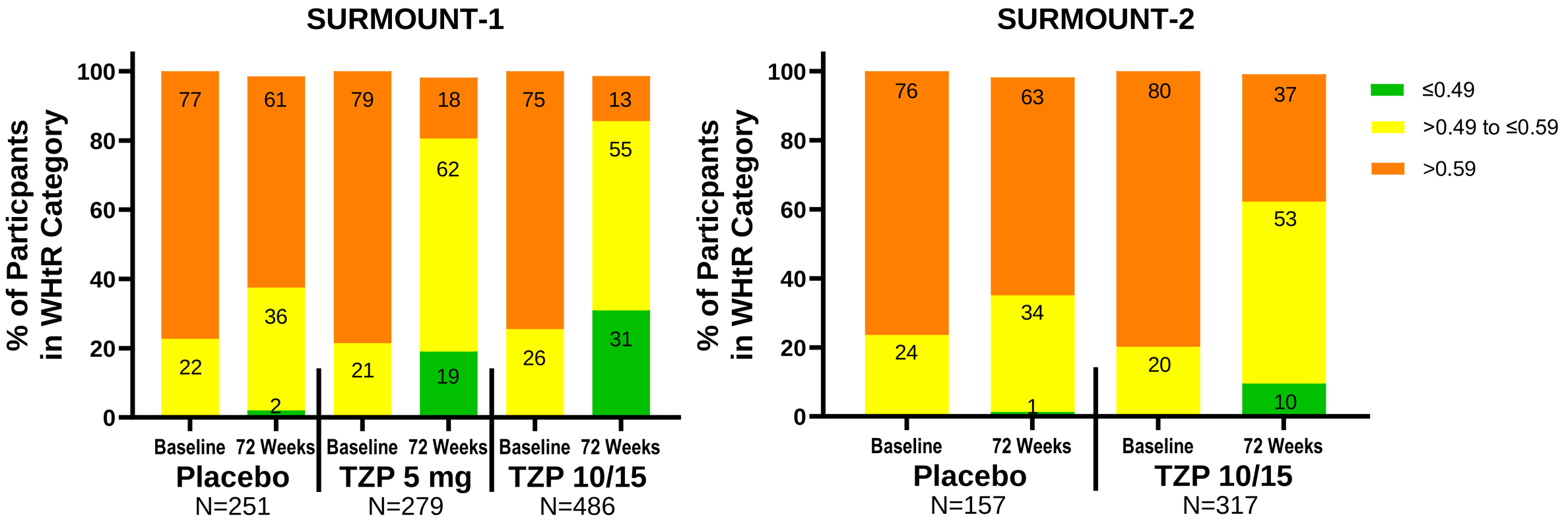
Treatment With Tirzepatide Was Associated With Shifts in WHtR Risk Categories from Baseline to Week 72 in Participants with BMI <35 kg/m^2

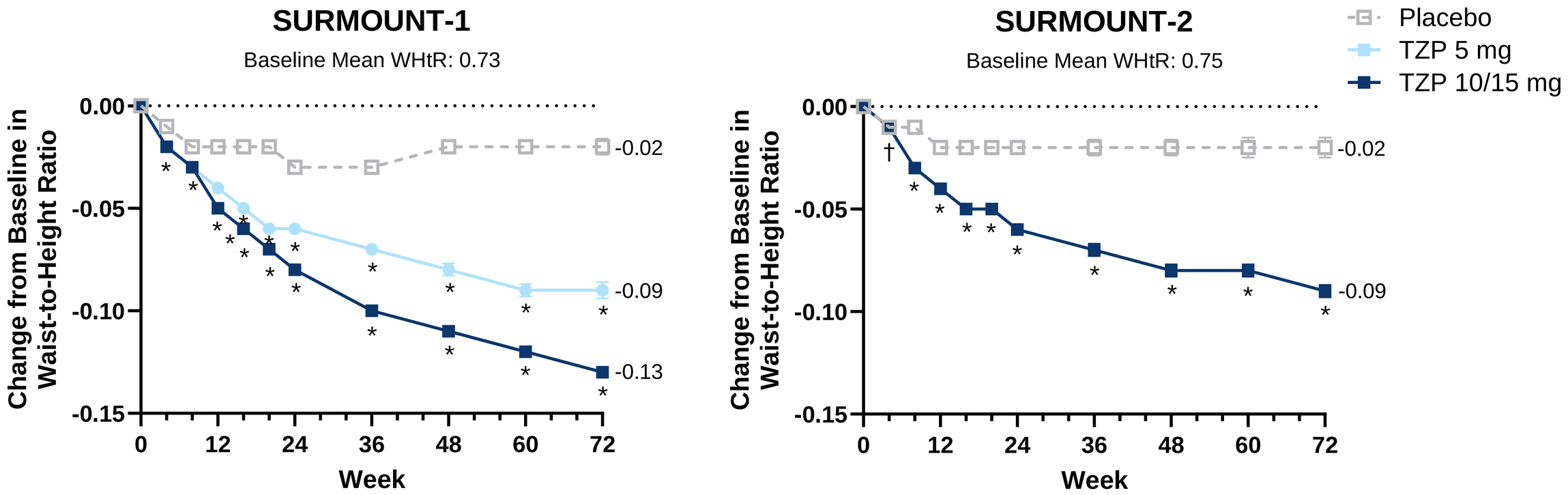
- 31% of participants treated with tirzepatide 10/15 mg in SURMOUNT-1 and 10% in SURMOUNT-2 achieved WHtR ≤0.49.



Note: There were 16 missing postbaseline values for SURMOUNT-1 and 6 for SURMOUNT-2. N= number of participants, TZP = tirzepatide.

Change from Baseline to Week 72 in WHtR Over Time in Participants with BMI ≥35 kg/m^2

- Treatment with tirzepatide was associated with a significant reduction of WHtR compared to placebo at Week 72



†p=0.04 tirzepatide vs. placebo. *p<0.001 tirzepatide vs. placebo. Data are least square means change from baseline. TZP = tirzepatide

CONCLUSIONS

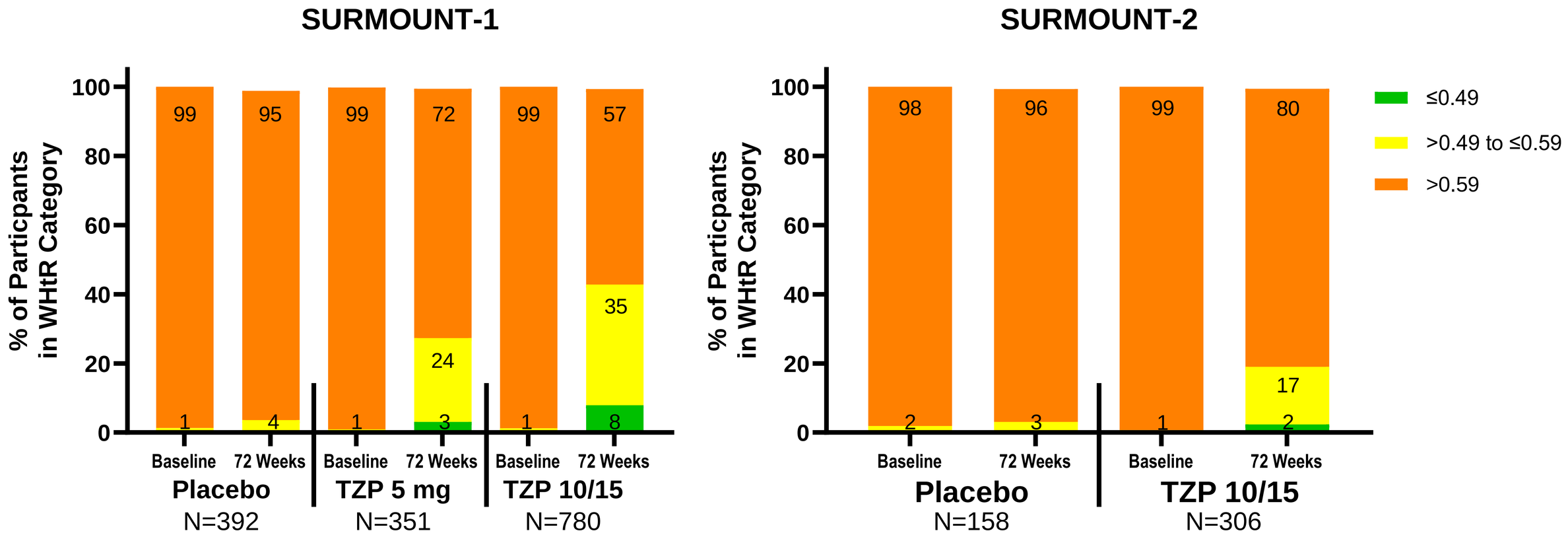
- In this post hoc analysis, treatment with tirzepatide in participants with BMI <35 kg/m^2 was associated with:
  - Significant reduction of WHtR
  - Shift to lower WHtR risk categories, with more individuals in “healthy,” fewer in “high,” and more moving from “high” to “increased” categories.
- In this post hoc analysis, treatment with tirzepatide in participants with BMI ≥35 kg/m^2 was associated with:
  - Similar magnitudes of WHtR reduction as seen in participants with BMI <35 kg/m^2; however, shifts to the healthy WHtR risk category was minimal.
- Future studies could further elucidate the effect of tirzepatide on other cardiometabolic parameters and outcomes and examine how changes in WHtR may explain any such benefits.

DISCLOSURES

- This study was sponsored by Eli Lilly and Company.
- ClinicalTrial.gov Identifiers NCT04184622, NCT04657003
- Beverly Tchang is an advisor to Novo Nordisk and Palatin Technologies
- NS has consulted for and/or received speaker honoraria from Abbott Laboratories, AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly and Company, Hanmi Pharmaceuticals, Janssen, Menarini-Ricerche, Novartis, Novo Nordisk, Pfizer, Roche Diagnostics, and Sanofi; and received grant support paid to his University from AstraZeneca, Boehringer Ingelheim, Novartis, and Roche Diagnostics.
- Hui Wang is an employee of TechData Services and contracted with Eli Lilly and Company to provide statistical analysis.
- Julia Dunn, Xiaotian Michelle Zhang, Luis-Emilio Garcia-Perez, Casey J. Mast, and Julia Fraseur Brumm are employees and shareholders of Eli Lilly and Company.

Back-ups

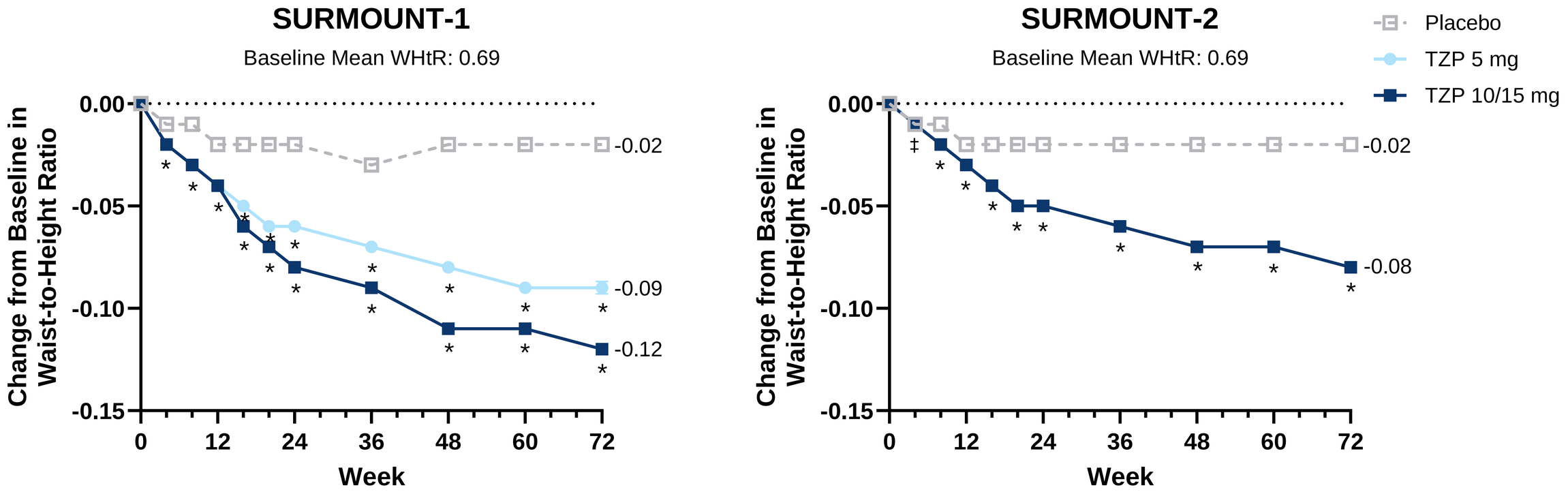
Shifts in WHtR Risk Categories from Baseline to Week 72 in Participants with BMI ≥35 kg/m^2



Note: There were 10 missing postbaseline values for SURMOUNT-1 and 3 for SURMOUNT-2. N= number of participants, TZP = tirzepatide.

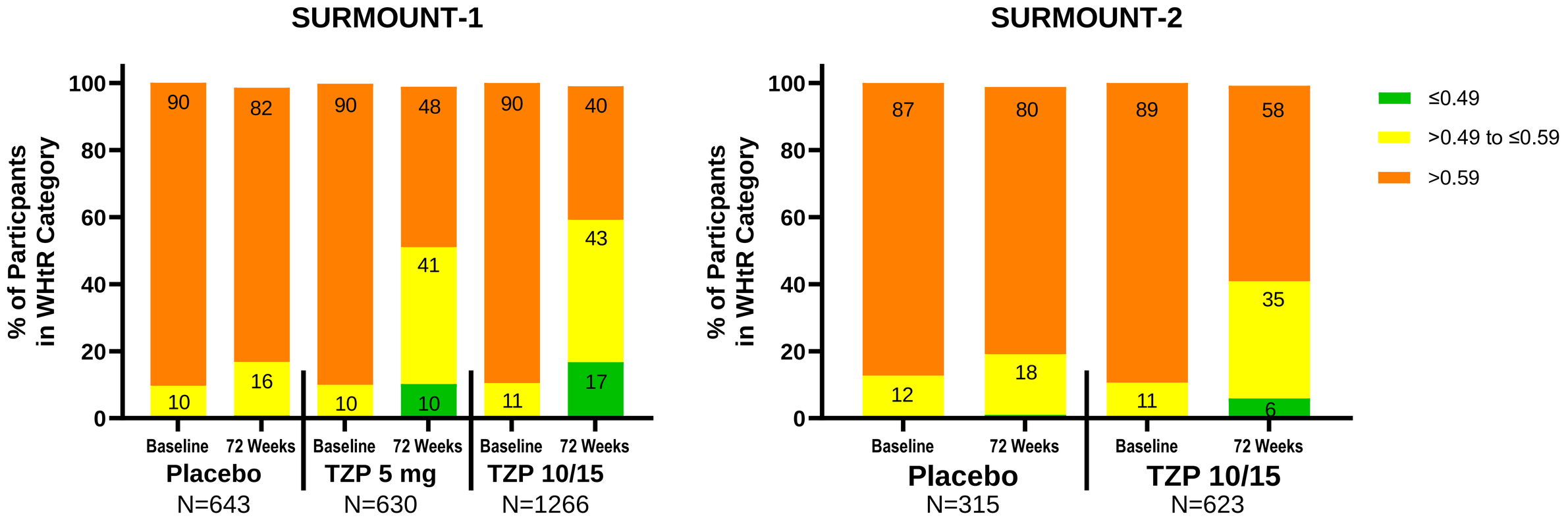
Change from Baseline to Week 72 in WHtR Over Time in All Participants

- Treatment with tirzepatide was associated with a significant reduction of WHtR compared to placebo at Week 72



‡p=0.01 tirzepatide vs. placebo. *p<0.001 tirzepatide vs. placebo. Data are least square means change from baseline. TZP = tirzepatide

Shifts in WHtR Risk Categories from Baseline to Week 72 in All Participants



Note: There were 21 missing postbaseline values for SURMOUNT-1 and 9 for SURMOUNT-2. N= number of participants, TZP = tirzepatide.