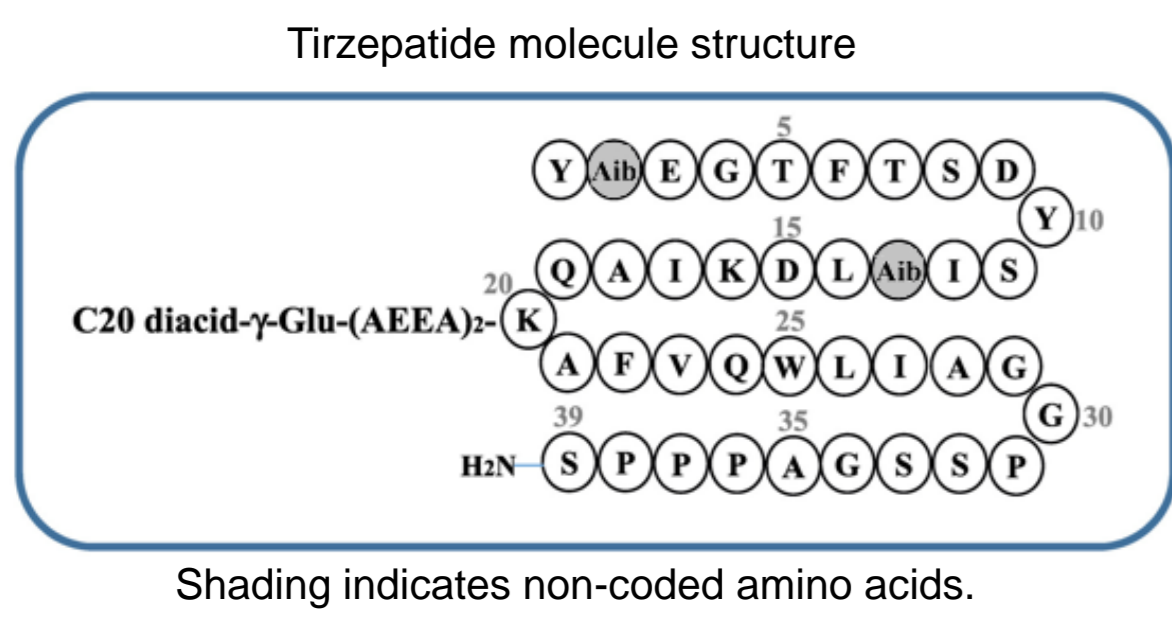


Relationship Between Body Weight Change and Glycemic Control with Tirzepatide Treatment in People with Type 2 Diabetes

Sue D. Pedersen¹, Guillermo Umpierrez², Francesco Giorgino³, Angel Rodriguez⁴, Vivian T. Thieu⁴, Ross Bray⁴, Helene Sapin⁴, Laura Fernández Landó⁴, Chrisanthi A. Karanikas⁴, Jacek Kiljanski⁴, C. Brock Woodis (Non-author presenter)⁴
¹C-ENDO Diabetes and Endocrinology Clinic, Calgary, Canada; ²Division of Endocrinology, Emory University School of Medicine, Atlanta, GA, USA; ³Department of Emergency and Organ Transplantation, University of Bari Aldo Moro, Bari, Italy; ⁴Eli Lilly and Company, Indianapolis, USA

BACKGROUND

- Tirzepatide is a once weekly GIP/GLP-1 receptor agonist approved for treatment of people with type 2 diabetes (T2D)

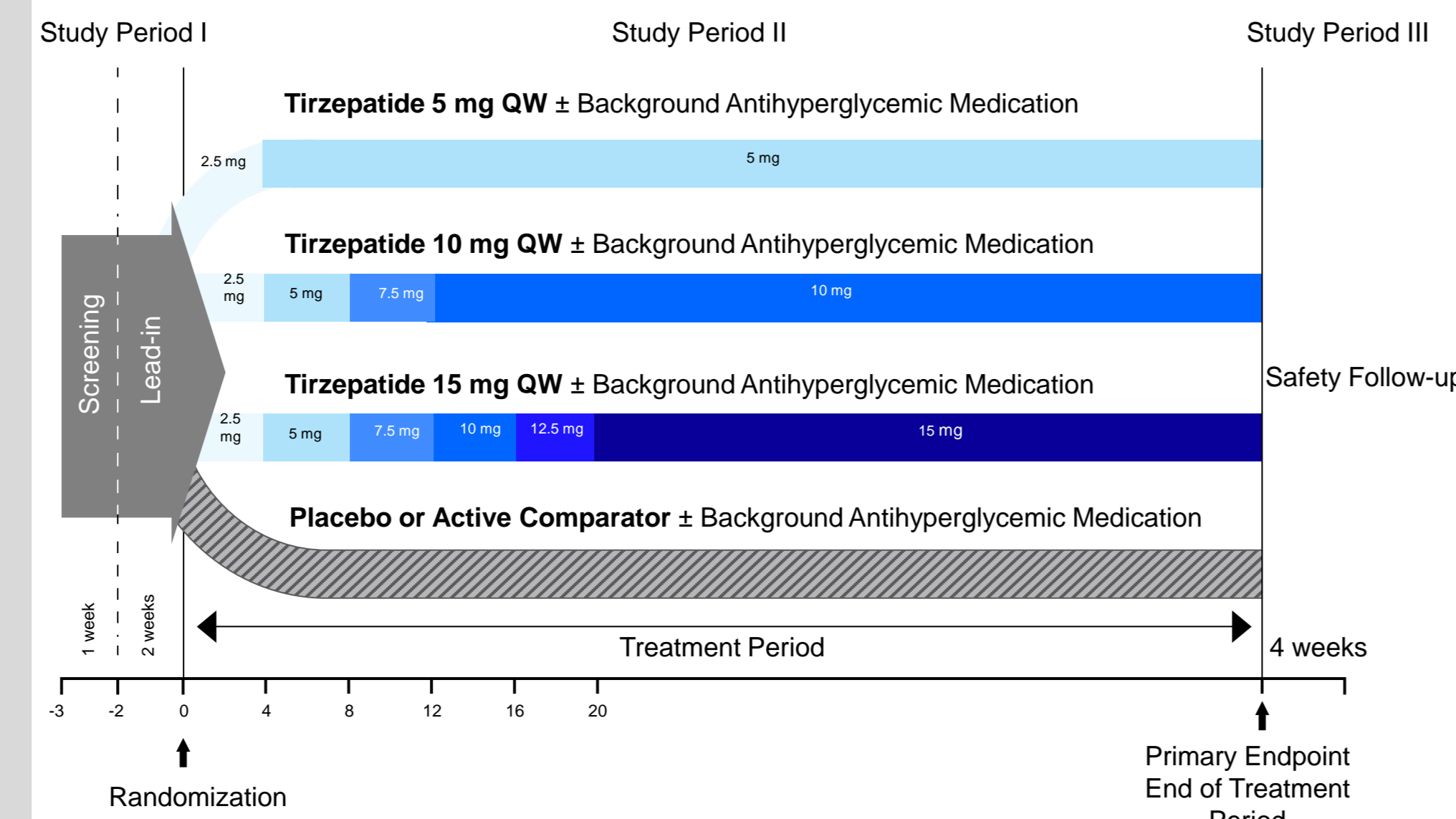


- In Phase 3 clinical trials, tirzepatide produced substantial reductions in HbA1c and body weight, enabling many people with T2D to achieve normalization of glucose control¹⁻⁵

OBJECTIVE

This post hoc analysis assessed the relationship between HbA1c and body weight reductions with tirzepatide treatment (5 mg, 10 mg or 15 mg) across the SURPASS-1 through -5 clinical trials.

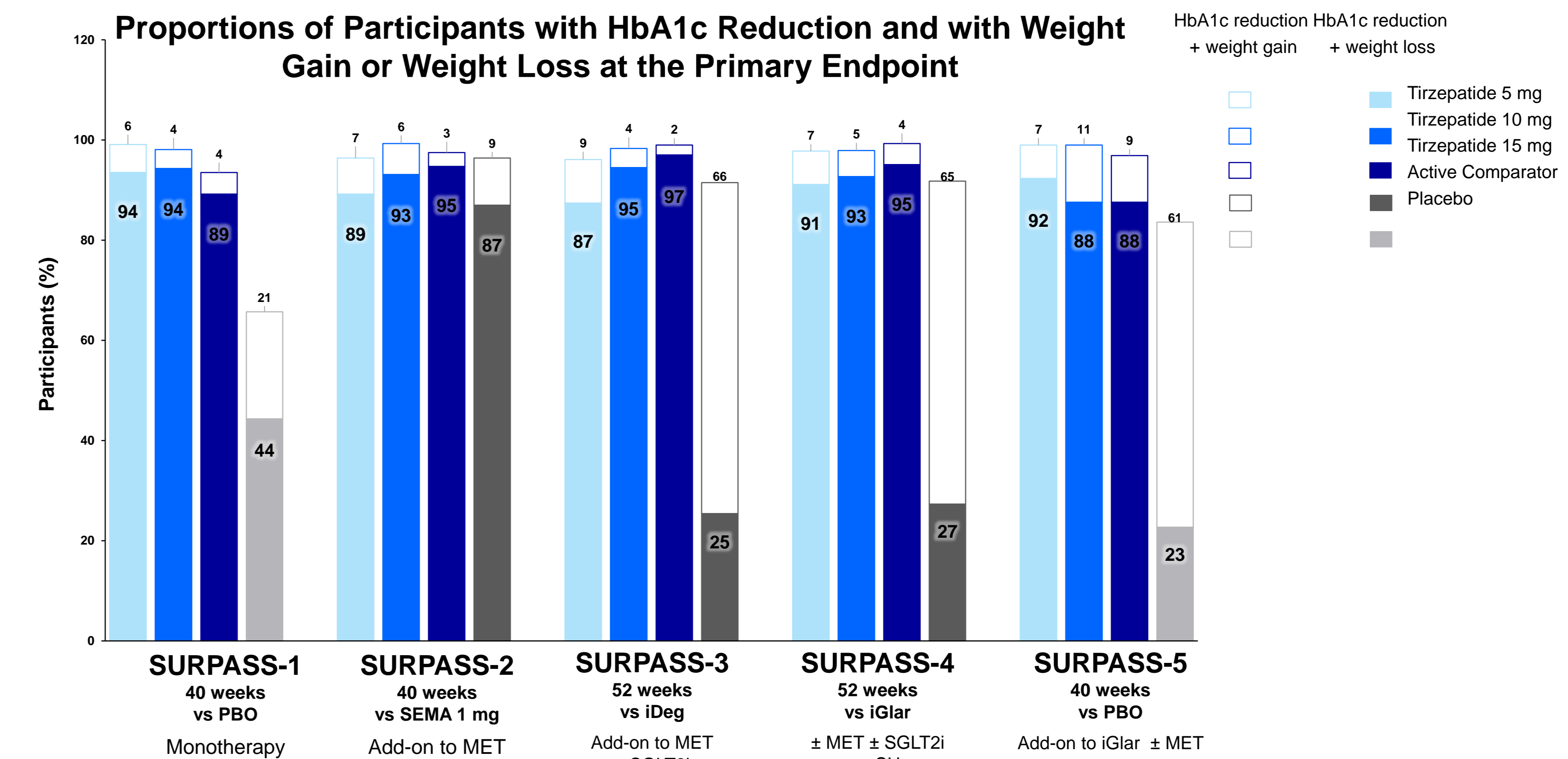
SURPASS STUDY DESIGN



Post hoc analysis: HbA1c and body weight data at 40 weeks (SURPASS-1, -2 and -5) and 52 weeks (SURPASS-3 and -4) were analyzed by trial, due to differences in design, background therapy, and baseline characteristics of participants

KEY RESULT

- Across the SURPASS trials,
 - Participants who experienced HbA1c reductions from baseline:
 - Tirzepatide 5 mg: 96-99%
 - Tirzepatide 10 mg: 98-99%
 - Tirzepatide 15 mg: 94-99%
 - Participants who experienced HbA1c reductions with weight loss:
 - Tirzepatide 5 mg: 87-94%
 - Tirzepatide 10 mg: 88-95%
 - Tirzepatide 15 mg: 88-97%



Data are presented as the proportion of participants with HbA1c reduction + weight loss (solid bars) and HbA1c reduction + weight gain (open bars). Observed values from participants on treatment at the primary endpoint visit in the mITT population, excluding participants who initiated rescue medication or discontinued treatment due to inadvertent enrollment. Note: Change from baseline in HbA1c reductions and weight loss or gain was defined as any change at the primary endpoint. HbA1c reductions and weight changes may not equal 100.

CONCLUSION

- Across the SURPASS trials, 87-97% of participants treated with tirzepatide (5 mg, 10 mg, 15 mg) experienced HbA1c reduction with weight loss.
- Significant correlations between HbA1c and body weight changes were observed in SURPASS-2, -3, -4 (all doses) and -5 (tirzepatide 5 mg only) regardless of background diabetes medications.

Correlations Between Changes from Baseline in HbA1c and Body Weight

SURPASS-1¹ 40 weeks, vs Placebo Monotherapy

Baseline characteristic, mean (SD) Change from baseline, LSM (SE), EAS	TZP 5 mg N=121	TZP 10 mg N=121	TZP 15 mg N=121	PBO N=115
Duration of diabetes, years	4.6 (5.1)	4.9 (5.6)	4.8 (5.0)	4.5 (5.9)
HbA1c, %	7.97 (0.8)	7.90 (0.8)	7.85 (1.0)	8.05 (0.8)
Change at 40 weeks, %	-1.87 (0.1) ^{##}	-1.89 (0.1) ^{##}	-2.07 (0.1) ^{##}	0.04 (0.1)
Body weight, kg	87.0 (21.2)	86.2 (19.5)	85.4 (18.5)	84.8 (20.0)
Change at 40 weeks, kg	-7.0 (0.5) ^{##}	-7.8 (0.5) ^{##}	-9.5 (0.5) ^{##}	-0.7 (0.6)

SURPASS-2² 40 weeks, vs Semaglutide 1 mg Add-on to MET

Baseline characteristic, mean (SD) Change from baseline, LSM (SE), EAS	TZP 5 mg N=470	TZP 10 mg N=469	TZP 15 mg N=470	SEMA 1 mg N=469
Duration of diabetes, years	9.1 (7.2)	8.4 (5.9)	8.7 (6.9)	8.3 (5.8)
HbA1c, %	8.32 (1.1)	8.30 (1.0)	8.26 (1.0)	8.25 (1.0)
Change at 40 weeks, %	-2.09 (0.1) ^{##}	-2.37 (0.1) ^{##}	-2.46 (0.1) ^{##}	-1.86 (0.1)
Body weight, kg	92.5 (21.8)	94.8 (22.7)	93.8 (21.8)	93.7 (21.1)
Change at 40 weeks, kg	-7.8 (0.3) ^{##}	-10.3 (0.3) ^{##}	-12.4 (0.3) ^{##}	-6.2 (0.3)

SURPASS-3³ 52 weeks, vs Insulin Degludec Add-on to MET ± SGLT2i

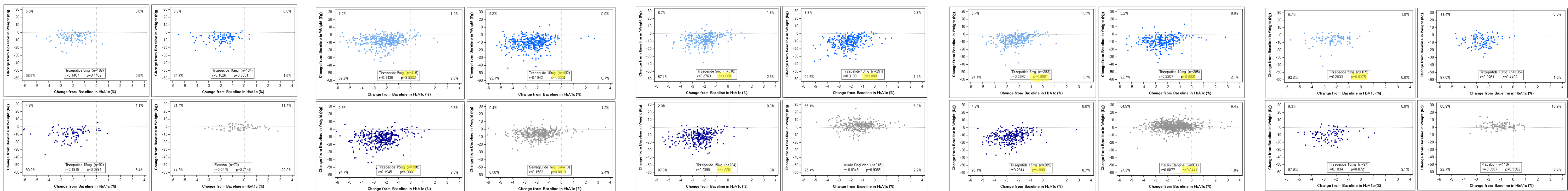
Baseline characteristic, mean (SD) Change from baseline, LSM (SE), EAS	TZP 5 mg N=358	TZP 10 mg N=360	TZP 15 mg N=359	iDeg N=360
Duration of diabetes, years	8.5 (5.8)	8.4 (6.6)	8.5 (6.5)	8.1 (6.0)
HbA1c, %	8.17 (0.9)	8.18 (0.9)	8.21 (0.9)	8.12 (0.9)
Change at 52 weeks, %	-1.93 (0.1) ^{##}	-2.20 (0.1) ^{##}	-2.37 (0.1) ^{##}	-1.34 (0.1)
Body weight, kg	94.4 (18.9)	93.8 (19.8)	94.9 (21.0)	94.0 (20.6)
Change at 52 weeks, kg	-7.5 (0.4) ^{##}	-10.7 (0.4) ^{##}	-12.9 (0.4) ^{##}	2.3 (0.4)

SURPASS-4⁴ 52 weeks, vs Insulin Glargine ± MET ± SGLT2i ± SU

Baseline characteristic, mean (SD) Change from baseline, LSM (SE), EAS	TZP 5 mg N=329	TZP 10 mg N=328	TZP 15 mg N=338	iGlar N=1000
Duration of diabetes, years	11.1 (7.1)	12.0 (7.5)	11.5 (7.5)	12.0 (7.7)
HbA1c, %	8.52 (0.8)	8.59 (0.9)	8.52 (1.0)	8.50 (0.9)
Change at 52 weeks, %	-2.24 (0.1) ^{##}	-2.43 (0.1) ^{##}	-2.58 (0.1) ^{##}	-1.44 (0.0)
Body weight, kg	90.3 (20.3)	90.6 (18.2)	90.0 (16.3)	90.2 (19.0)
Change at 52 weeks, kg	-7.1 (0.3) ^{##}	-9.5 (0.3) ^{##}	-11.7 (0.3) ^{##}	1.9 (0.2)

SURPASS-5⁵ 40 weeks, vs Placebo Add-on to iGlar ± MET

Baseline characteristic, mean (SD) Change from baseline, LSM (SE), EAS	TZP 5 mg N=116	TZP 10 mg N=119	TZP 15 mg N=120	PBO N=120
Duration of diabetes, years	14.1 (8.1)	12.6 (6.2)	13.7 (7.5)	12.9 (7.4)
HbA1c, %	8.30 (0.9)	8.36 (0.8)	8.23 (0.9)	8.37 (0.8)
Change at 40 weeks, %	-2.23 (0.1) ^{##}	-2.59 (0.1) ^{##}	-2.59 (0.1) ^{##}	-0.93 (0.1)
Body weight, kg	95.8 (19.8)	94.5 (22.2)	96.3 (22.8)	94.1 (21.8)
Change at 40 weeks, kg	-6.2 (0.6) ^{##}	-8.2 (0.6) ^{##}	-10.9 (0.6) ^{##}	1.7 (0.6)



- Correlations between HbA1c and body weight changes were observed with tirzepatide in SURPASS-2, -3, -4 (all doses) and -5 (tirzepatide 5 mg only) (statistically significant correlation coefficients ranged from 0.1438 to 0.3130 across studies; p<0.038, for all doses highlighted in yellow)

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For more information, please contact Vivian Thieu (thieu.vivian.thuyanh@lilly.com)
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Data are LSM, unless otherwise noted (MMRM; efficacy estimand). ^{##}p<0.001 vs comparator. Abbreviations: EAS = efficacy analysis set; HbA1c = glycosylated hemoglobin A1c; iDeg = insulin degludec; iGlar = insulin glargine; MET = metformin; mITT = modified intent-to-treat; PBO = placebo; SEMA = semaglutide; SGLT2i = sodium-glucose cotransporter-2 inhibitor; SU = sulfonylurea; TZP = tirzepatide; vs - versus.
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