

SUPPLEMENTARY MATERIAL**Association Between Early Weight Loss and Metabolic Outcomes with Tirzepatide in Japanese Patients with Type 2 Diabetes: A SURPASS J Post Hoc Analysis**

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Table S1. Univariate logistic regression analysis of baseline factors associated with achievement of $\geq 5\%$ weight loss at week 8 in the SURPASS J studies

Factor	OR ^a (95% CI)	p value
Sex		
Female vs. male	1.46 (1.03, 2.06)	<0.05
Age, years	1.02 (1.00, 1.03)	<0.05
Diabetes duration, years	0.98 (0.95, 1.00)	0.104
HbA _{1c} , %	0.67 (0.56, 0.79)	<0.05
FSG, mg/dL	0.99 (0.98, 0.99)	<0.05
Weight, kg	0.96 (0.95, 0.97)	<0.05
BMI, kg/m ²	0.89 (0.85, 0.93)	<0.05
Waist circumference, cm	0.95 (0.93, 0.97)	<0.05
eGFR (CKD-EPI), mL/min/1.73 m ²	0.99 (0.97, 1.00)	<0.05
SBP, mmHg	1.00 (0.99, 1.01)	0.917
DBP, mmHg	0.99 (0.97, 1.00)	0.130
Triglycerides, mg/dL	1.00 (1.00, 1.00)	0.617
HDL-C, mg/dL	1.00 (0.99, 1.01)	0.816
OAM use ^b		
Any OAM vs. no use	0.85 (0.62, 1.16)	0.298
Alpha-glucosidase inhibitors vs. no use	2.13 (1.23, 3.61)	<0.05
Biguanides vs. no use	1.01 (0.53, 1.84)	0.968
Glinides vs. no use	0.70 (0.34, 1.32)	0.298
SGLT2is vs. no use	1.12 (0.60, 1.97)	0.715
Sulfonylureas vs. no use	0.46 (0.26, 0.77)	<0.05
Thiazolidinediones vs. no use	0.89 (0.46, 1.64)	0.727

Overall $N=893$. Only participants with weight data available at week 8 were included in the analysis. Data are pooled from the tirzepatide-treated participants from the SURPASS J-mono and J-combo studies. Variables showing statistical significance in univariate analysis were included in the multivariate model. *BMI* body mass index, *CI* confidence interval, *CKD-EPI* Chronic Kidney Disease-Epidemiology Collaboration, *DBP* diastolic blood pressure, *eGFR* estimated glomerular filtration rate, *FSG* fasting serum glucose, *HbA_{1c}* glycated hemoglobin, *HDL-C* high-density lipoprotein cholesterol, *OAM* oral

antihyperglycemic medication, *OR* odds ratio, *SBP* systolic blood pressure, *SGLT2is* sodium-glucose cotransporter 2 inhibitors.

^aFor continuous variables, the OR of achieving $\geq 5\%$ reduction in body weight at week 8 per 1-increment increase in the variable is presented.

^bParticipants in SURPASS J-combo had received OAM monotherapy for ≥ 3 months at baseline and continued their background OAM regimen throughout treatment.

Table S2. Change from baseline in body mass parameters by weight loss achievement at 8 weeks

Variable	Tirzepatide 5 mg			Tirzepatide 10 mg			Tirzepatide 15 mg			Overall		
	Weight loss ≥5%	Weight loss <5%	LSM difference	Weight loss ≥5%	Weight loss <5%	LSM difference	Weight loss ≥5%	Weight loss <5%	LSM difference	Weight loss ≥5%	Weight loss <5%	LSM difference
Change in body weight, %	N=71	N=225		N=67	N=232		N=72	N=226		N=210	N=683	
4 weeks	-3.5 (0.2)	-0.8 (0.1)	-2.8***	-3.1 (0.2)	-0.9 (0.1)	-2.2***	-3.2 (0.2)	-0.8 (0.1)	-2.4***	-3.3 (0.1)	-0.8 (0.1)	-2.4***
8 weeks	-7.1 (0.2)	-2.1 (0.1)	-5.1***	-7.1 (0.2)	-2.0 (0.1)	-5.0***	-6.7 (0.2)	-1.9 (0.1)	-4.8***	-7.0 (0.1)	-2.0 (0.1)	-5.0***
12 weeks	-8.9 (0.3)	-2.8 (0.2)	-6.1***	-9.5 (0.3)	-3.6 (0.1)	-5.9***	-9.3 (0.3)	-3.3 (0.2)	-6.0***	-9.2 (0.2)	-3.2 (0.1)	-6.0***
16 weeks	-10.1 (0.3)	-3.0 (0.2)	-7.0***	-11.9 (0.4)	-5.0 (0.2)	-6.9***	-11.7 (0.4)	-4.7 (0.2)	-7.0***	-11.2 (0.2)	-4.3 (0.1)	-6.9***
20 weeks	-11.2 (0.4)	-3.1 (0.2)	-8.0***	-13.3 (0.5)	-5.9 (0.2)	-7.3***	-14.0 (0.5)	-6.0 (0.3)	-8.0***	-12.8 (0.3)	-5.0 (0.1)	-7.8***
24 weeks	-11.6 (0.4)	-3.4 (0.2)	-8.2***	-13.7 (0.6)	-6.6 (0.3)	-7.1***	-15.9 (0.6)	-7.5 (0.3)	-8.4***	-13.7 (0.3)	-5.8 (0.2)	-7.9***
32 weeks	-12.3 (0.5)	-3.7 (0.3)	-8.7***	-15.0 (0.7)	-7.6 (0.3)	-7.4***	-17.9 (0.7)	-9.3 (0.4)	-8.6***	-15.1 (0.4)	-6.8 (0.2)	-8.2***
40 weeks	-13.0 (0.6)	-4.0 (0.3)	-9.0***	-15.6 (0.8)	-8.2 (0.4)	-7.5***	-19.4 (0.8)	-10.2 (0.4)	-9.2***	-16.0 (0.5)	-7.5 (0.2)	-8.5***
48 weeks	-13.2 (0.7)	-4.2 (0.4)	-9.1***	-16.2 (0.8)	-8.5 (0.4)	-7.7***	-19.9 (0.8)	-11.1 (0.5)	-8.8***	-16.4 (0.5)	-7.9 (0.3)	-8.5***
52 weeks	-13.8 (0.7)	-4.1 (0.4)	-9.6***	-16.5 (0.8)	-8.8 (0.4)	-7.7***	-20.0 (0.9)	-11.5 (0.5)	-8.5***	-16.7 (0.5)	-8.1 (0.3)	-8.6***
Change in BMI, kg/m²	N=71	N=225		N=67	N=232		N=72	N=226		N=210	N=683	
4 weeks	-1.0 (0.0)	-0.2 (0.0)	-0.7***	-0.9 (0.1)	-0.3 (0.0)	-0.6***	-0.8 (0.1)	-0.2 (0.0)	-0.6***	-0.9 (0.0)	-0.2 (0.0)	-0.7***
8 weeks	-1.9 (0.1)	-0.6 (0.0)	-1.3***	-1.9 (0.1)	-0.6 (0.0)	-1.3***	-1.8 (0.1)	-0.5 (0.0)	-1.3***	-1.9 (0.0)	-0.6 (0.0)	-1.3***
12 weeks	-2.4 (0.1)	-0.8 (0.1)	-1.6***	-2.6 (0.1)	-1.0 (0.0)	-1.6***	-2.5 (0.1)	-0.9 (0.1)	-1.5***	-2.5 (0.1)	-0.9 (0.0)	-1.6***
16 weeks	-2.7 (0.1)	-0.8 (0.1)	-1.9***	-3.2 (0.1)	-1.4 (0.1)	-1.8***	-3.1 (0.1)	-1.3 (0.1)	-1.8***	-3.0 (0.1)	-1.2 (0.0)	-1.8***
20 weeks	-3.0 (0.1)	-0.9 (0.1)	-2.1***	-3.6 (0.1)	-1.6 (0.1)	-2.0***	-3.7 (0.1)	-1.7 (0.1)	-2.0***	-3.4 (0.1)	-1.4 (0.0)	-2.0***
24 weeks	-3.1 (0.1)	-0.9 (0.1)	-2.2***	-3.7 (0.2)	-1.8 (0.1)	-1.9***	-4.2 (0.2)	-2.1 (0.1)	-2.1***	-3.7 (0.1)	-1.6 (0.1)	-2.0***
32 weeks	-3.3 (0.2)	-1.0 (0.1)	-2.3***	-4.1 (0.2)	-2.1 (0.1)	-2.0***	-4.8 (0.2)	-2.6 (0.1)	-2.1***	-4.0 (0.1)	-1.9 (0.1)	-2.1***
40 weeks	-3.5 (0.2)	-1.1 (0.1)	-2.4***	-4.2 (0.2)	-2.3 (0.1)	-2.0***	-5.2 (0.2)	-2.9 (0.1)	-2.3***	-4.3 (0.1)	-2.1 (0.1)	-2.2***
48 weeks	-3.6 (0.2)	-1.1 (0.1)	-2.4***	-4.4 (0.2)	-2.4 (0.1)	-2.0***	-5.3 (0.2)	-3.2 (0.1)	-2.1***	-4.4 (0.1)	-2.2 (0.1)	-2.2***
52 weeks	-3.7 (0.2)	-1.1 (0.1)	-2.6***	-4.5 (0.2)	-2.5 (0.1)	-2.0***	-5.3 (0.3)	-3.3 (0.1)	-2.1***	-4.5 (0.1)	-2.3 (0.1)	-2.2***
Change in waist circumference, cm	N=71	N=225		N=67	N=231		N=72	N=225		N=210	N=681	
4 weeks	-1.2 (0.3)	-0.6 (0.2)	-0.7	-1.2 (0.3)	-0.6 (0.2)	-0.6	-1.5 (0.3)	-0.4 (0.2)	-1.1**	-1.3 (0.2)	-0.5 (0.1)	-0.8***
8 weeks	-3.2 (0.3)	-1.3 (0.2)	-1.9***	-3.5 (0.4)	-1.4 (0.2)	-2.1***	-3.9 (0.4)	-1.3 (0.2)	-2.6***	-3.6 (0.2)	-1.4 (0.1)	-2.2***
12 weeks	-5.0 (0.4)	-1.8 (0.2)	-3.2***	-5.9 (0.4)	-2.1 (0.2)	-3.8***	-6.0 (0.4)	-2.3 (0.2)	-3.7***	-5.7 (0.2)	-2.1 (0.1)	-3.6***
16 weeks	-6.1 (0.4)	-2.2 (0.2)	-3.9***	-7.2 (0.5)	-3.1 (0.2)	-4.2***	-7.7 (0.4)	-3.1 (0.2)	-4.6***	-7.0 (0.3)	-2.8 (0.1)	-4.2***
20 weeks	-6.9 (0.5)	-2.4 (0.3)	-4.5***	-8.5 (0.5)	-4.0 (0.3)	-4.5***	-10.2 (0.5)	-4.0 (0.3)	-6.2***	-8.6 (0.3)	-3.5 (0.2)	-5.1***

Variable	Tirzepatide 5 mg			Tirzepatide 10 mg			Tirzepatide 15 mg			Overall		
	Weight loss ≥5%	Weight loss <5%	LSM difference	Weight loss ≥5%	Weight loss <5%	LSM difference	Weight loss ≥5%	Weight loss <5%	LSM difference	Weight loss ≥5%	Weight loss <5%	LSM difference
24 weeks	-7.6 (0.5)	-2.6 (0.2)	-5.0***	-8.6 (0.6)	-4.5 (0.3)	-4.0***	-11.3 (0.5)	-5.0 (0.3)	-6.3***	-9.2 (0.3)	-4.0 (0.2)	-5.1***
32 weeks	-8.3 (0.5)	-2.6 (0.3)	-5.6***	-9.5 (0.6)	-5.4 (0.3)	-4.2***	-13.0 (0.7)	-6.4 (0.3)	-6.6***	-10.3 (0.4)	-4.8 (0.2)	-5.5***
40 weeks	-8.7 (0.6)	-2.9 (0.3)	-5.8***	-10.4 (0.6)	-5.3 (0.3)	-5.1***	-14.2 (0.7)	-6.9 (0.4)	-7.2***	-11.0 (0.4)	-5.0 (0.2)	-6.0***
48 weeks	-8.8 (0.6)	-2.9 (0.3)	-5.9***	-11.1 (0.7)	-5.8 (0.3)	-5.3***	-14.2 (0.7)	-7.5 (0.4)	-6.7***	-11.4 (0.4)	-5.4 (0.2)	-6.0***
52 weeks	-9.3 (0.7)	-2.9 (0.4)	-6.3***	-11.3 (0.7)	-5.8 (0.4)	-5.5***	-14.4 (0.8)	-7.8 (0.4)	-6.7***	-11.7 (0.4)	-5.5 (0.2)	-6.2***

Data are LSM (standard error) unless otherwise indicated. Data were pooled from SURPASS J-mono and J-combo participants who were randomized to tirzepatide and took ≥1 dose. Participants were included if they were on treatment at week 8 and had body weight data available at week 8. Statistical analysis was performed using a mixed model for repeated measures.

BMI body mass index, *LSM* least-squares mean, *N* number of participants in the population with a baseline and postbaseline value at the specified time point.

** $p < 0.01$; *** $p < 0.001$.

Table S3. Use of concomitant antihypertensive drugs and lipid-lowering drugs in SURPASS J studies by weight-loss subgroups

Concomitant medication	Weight loss $\geq 5\%$ subgroup			Weight loss $< 5\%$ subgroup		
	TZP 5 mg N = 65	TZP 10 mg N = 56	TZP 15 mg N = 55	TZP 5 mg N = 215	TZP 10 mg N = 215	TZP 15 mg N = 206
Antihypertensive drug use at baseline	30 (46.2%)	20 (35.7%)	19 (34.5%)	100 (46.5%)	94 (43.7%)	96 (46.6%)
Antihypertensive drug use at Week 52	32 (49.2%)	19 (33.9%)	16 (29.1%)	101 (47.0%)	93 (43.3%)	92 (44.7%)
Lipid-lowering drug use at baseline	25 (38.5%)	29 (51.8%)	20 (36.4%)	102 (47.4%)	104 (48.4%)	83 (40.3%)
Lipid-lowering drug use at Week 52	24 (36.9%)	29 (51.8%)	18 (32.7%)	103 (47.9%)	104 (48.4%)	81 (39.3%)

Data are shown as n (%). TZP, tirzepatide