## Presenter Disclosure

## PRESENTER DISCLOSURE



- Ariana M. Chao, PhD, CRNP, RN
- Advisory Panel/Consultant: Boehringer Ingelheim; Eli Lilly and Company
- Research Support: Eli Lilly and Company; National Institutes of Health

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**Body Weight Reduction Associated With** Tirzepatide by Sex: A Subgroup Analysis of the **SURMOUNT Clinical Trials** 

> Ariana Chao<sup>1</sup>, Rebecca Taylor<sup>2</sup>, Donna Mojdami<sup>2</sup>, Tammy Forrester<sup>2</sup>, Farai Chigutsa<sup>2</sup>, and Raleigh Malik<sup>2</sup>



## **Sex Differences in Obesity and Treatment** Outcomes

Prevalence Percentage of BMI ≥30 kg/m<sup>2</sup> From NHANES 2017–March 2020



BMI, body mass index; NHANES, National Health and Nutrition Examination Survey. Stierman B, et al. Natl Health Stat Rep. 2021;58:1–21; Williams RL, et al. Obes Rev. 2015;16(2):171–186.

## **Sex Differences in Obesity and Treatment** Outcomes

Prevalence Percentage of BMI ≥40 kg/m<sup>2</sup> From NHANES 2017–March 2020



BMI, body mass index; NHANES, National Health and Nutrition Examination Survey. Stierman B, et al. Natl Health Stat Rep. 2021;58:1–21; Williams RL, et al. Obes Rev. 2015;16(2):171–186.

Percentage



## **Sex Differences in Obesity and Treatment** Outcomes

2017–March 2020



BMI, body mass index; NHANES, National Health and Nutrition Examination Survey. Stierman B, et al. Natl Health Stat Rep. 2021;58:1–21; Williams RL, et al. Obes Rev. 2015;16(2):171–186.

## Background

- and overweight, with or without type 2 diabetes
- study participants

Tirzepatide is a once-weekly glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptor agonist

Treatment with tirzepatide in the SURMOUNT-1 to -4 trials demonstrated efficacy in weight reduction in adults with obesity

A post hoc subgroup analysis was conducted to determine if the weight-lowering observations with tirzepatide varied by the sex of

### SURMOUNT-1

Tirzepatide 5

Tirzepatide 10

Tirzepatide 15

Placebo

\*MTD, maximal tolerated dose (10 mg or 15 mg).

5 mg	Obesity Manage
0 mg	N=2539 (1714 females; 825 m Duration: 72 v
5 mg	Additional 2-year treatment period for patients with predia
	Jastreboff et al. N Engl J Med. 2022;387(3):205



### SURMOUNT-1

SURMOUNT-2

Tirzepatide 5

Tirzepatide 10

Tirzepatide 1

Placebo

Tirzepatide 10

Tirzepatide 15

Placebo

\*MTD, maximal tolerated dose (10 mg or 15 mg).

5 mg	Obesity Manage
0 mg	N=2539 (1714 females; 825 m Duration: 72 v
5 mg	Additional 2-year treatment period for patients with predia
)	Jastreboff et al. N Engl J Med. 2022;387(3):203
	Obesity Management With
0 mg	N=938 (476 females; 462 m
5 mg	Duration: 72 v
)	
	Garvey et al. Lancet. 2023;402(10402):61





\*MTD, maximal tolerated dose (10 mg or 15 mg).

Obesity Manage		5 mg
N=2539 (1714 females; 825 m Duration: 72 v		0 mg
Additional 2-year treatment period for patients with predia		5 mg
Jastreboff et al. N Engl J Med. 2022;387(3):205		
Obesity Management With N=938 (476 females; 462 m		0 mg
Duration: 72 v		5 mg
		)
Garvey et al. Lancet. 2023;402(10402):61		
Obesity Management After Intensive Lifestyle Pro		
Randomized N=579 (364 females; 215 m Duration: 84 v	Tirzepatide MTD*	Г
	Placebo	1
Wadden et al. Nat Med. 2023;29(11):2909		





\*MTD, maximal tolerated dose (10 mg or 15 mg).

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0 mg		N=938 (476 females; 462 m
5 mg		Duration: 72 w
)		
		Garvey et al. Lancet. 2023;402(10402):61
		Obesity Management After Intensive Lifestyle Pro
	Tirzepatide MTD*	Randomized N=579 (364 females; 215 m Duration: 84 w
1	Placebo	
		Wadden et al. Nat Med. 2023;29(11):2909
		<b>Weight Mainten</b> Randomized N=670 (473 females; 197 m
	Tirzepatide MTD*	Duration: 88 w
L	Placebo	
		Aronne et al. JAMA. 2024;331(1):



## Methods

- Participants in SURMOUNT-1 to -4 were categorized by sex
- randomization to:
  - Week 72 in SURMOUNT-1, -2, and -3, or
- measure

This exploratory analysis examined percent change in body weight, using a mixed model for repeated measures (MMRM), and the proportion of participants achieving  $\geq$ 5%,  $\geq$ 10%, and  $\geq$ 15% reductions in body weight, using logistic regression, from

• Week 88 (52 weeks after randomization) in SURMOUNT-4

Safety data were examined by study, with the various doses used (tirzepatide 5) mg, 10 mg, 15 mg and the maximum tolerated dose [MTD]) combined into a single

All analyses used the efficacy analysis data set (all randomized participants who received  $\geq 1$  dose of study treatment, excluding data after study drug discontinuation)

## **Baseline Characteristics**

	SURMOUNT-1 (N=2539)		SURMO (N=S		SURMO (N=		SURMOUNT-4 (N=670)		
	Females	Males	Females	Males	Females	Males	Females	Males	
Sex, n (%)	1714 (67.5)	825 (32.5)	476 (50.7)	462 (49.3)	364 (62.9)	215 (37.1)	473 (70.6)	197 (29.4)	
Age, mean, years	45.1	44.4	54.3	54.2	45.3	46.0	48.9	48.0	

N, number of participants; n, number of participants in subgroup; BMI, body mass index.

### The proportion of males ranged from 29.4% to 49.3% across studies.

## **Baseline Characteristics**

	SURMOUNT-1 (N=2539)		SURMC (N=S		SURMO (N=		SURMOUNT-4 (N=670)		
	Females	Males	Females	Males	Females	Males	Females	Males	
Sex, n (%)	1714 (67.5)	825 (32.5)	476 (50.7)	462 (49.3)	364 (62.9)	215 (37.1)	473 (70.6)	197 (29.4)	
Age, mean, years	45.1	44.4	54.3	54.2	45.3	46.0	48.9	48.0	
White race, n (%)	1275 (74.4)	517 (62.7)	371 (77.9)	339 (73.4)	303 (83.2)	195 (90.7)	375 (79.3)	162 (82.2)	
Body weight, mean, kg	99.8	115.2	94.8	106.8	95.4	112.9	79.6	98.6	
Waist circumference, mean, cm	111.2	120.2	113.3	116.7	104.9	117.3	94.2	105.4	
BMI, mean, kg/m <sup>2</sup>	38.2	37.6	36.7	35.4	36.1	35.8	30.1	31.4	

N, number of participants; n, number of participants in subgroup; BMI, body mass index.

## **Tirzepatide Was Associated With Significant Weight** Loss in Both Females and Males at All Doses

## **Percent Weight Change From Baseline**



Data are shown as least-squares mean (standard error). \* P<0.05 for tirzepatide vs placebo. Analysis of the percent change in body weight from baseline was conducted using an MMRM. SURMOUNT-4 results are based on change from randomization (week 36 to week 88). N, number of participants.

Males



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\_\_\_ -2.7

Placebo

## **Tirzepatide Was Associated With Significant Weight** Loss in Both Females and Males at All Doses

### Females Percent Weight Change From Baseline Males





Data are shown as least-squares mean (standard error). \* P<0.05 for tirzepatide vs placebo. Analysis of the percent change in body weight from baseline was conducted using an MMRM. SURMOUNT-4 results are based on change from randomization (week 36 to week 88). N, number of participants.

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SURMOUNT-3 SURMOUNT-4 (N=195)

## **Proportion Achieving ≥5% Weight Reduction**



\*P<0.05 for tirzepatide vs placebo. Analysis of the percent change in body weight from baseline was conducted using an MMRM. SURMOUNT-4 results are based on change from randomization (week 36 to week 88). N, number of participants.



### **Proportion Achieving ≥5% Weight Reduction**



to week 88). N, number of participants.

### Males **SURMOUNT-3** SURMOUNT-4 72 weeks 52 weeks (N=213) (N=195) \* 89.5 38.8 24.8 14.8

### **Proportion Achieving ≥10% Weight Reduction**



to week 88). N, number of participants.

### **Proportion Achieving ≥15% Weight Reduction**



\*P<0.05 for tirzepatide vs placebo. Analysis of the percent change in body weight from baseline was conducted using an MMRM. SURMOUNT-4 results are based on change from randomization (week 36) to week 88). N, number of participants.

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SURMOUNT-3 SURMOUNT-4

## Females Receiving Tirzepatide Lost More Weight **Than Males Receiving Tirzepatide**

### Differences in Percent Change in Body Weight for Tirzepatide Treatment Groups

		-		-				-			-				
	Study	Sex	Treatment	n								V	leight Loss		Test for
	SURMOUNT-1	Female	Placebo	309								_^	14.7 (-16.1, -13	84)	Treatmer
			Tirzepatide 5 mg	364									•		
_			Tirzepatide 10 mg	361									20.4 (-21.8, - 19	,	
			Tirzepatide 15 mg	360		H						-2	21.8 (-23.1, - 20	0.4)	
		Male	Placebo	162											
			Tirzepatide 5 mg	175								-´	10.9 (-12.6, -9.3	3)	
			Tirzepatide 10 mg	170								-1	15.7 (-17.4, -14	l.1)	
ſ			Tirzepatide 15 mg	175			F					- ´	16.5 (-18.1, -14	.8)	
	SURMOUNT-2	Female	Placebo	133											Treatmer
			Tirzepatide 10 mg	142								- ´	11.5 (-13.5, -9.6	6)	
			Tirzepatide 15 mg	133								-1	14.1 (-16.1, -12	2.2)	
		Male	Placebo	131											
			Tirzepatide 10 mg	140								-{	3.8 (-10.6, -7.0)	)	
			Tirzepatide 15 mg	132								-1	10.6 (-12.4, -8.8	8)	
	SURMOUNT-3	Female	Placebo	127											Treatmer
		i cinaic	Tirzepatide MTD	142								-2	27.6 (-29.7, -25	5 6)	
		Male	Placebo	75							1	-		)	
			Tirzepatide MTD	85								-1	18.9 (-21.3, -16	6.4)	
	SURMOUNT-4	Female	Placebo	191											Treatmer
			Tirzepatide MTD	211								-2	23.4 (-25.2, -21	.7)	
		Male	Placebo	82								_	,	,	
			Tirzepatide MTD	88								-1	16.9 (-19.3, -14	l.5)	
in w	eight loss with tirzer	patide			<b></b>		•••••	•••••	•••	•••	••••••	··· <u>·</u>			
k 72	2 for SURMOUNT-1	to -3 or			-30	-25	-20	-15	-10	-5	0	5			
	IOUNT-4.		<b>— — — —</b>		<b>•</b> -		•	-	•	Differer			<b>— —</b>	<b>.</b>	
SM,	least-squares mean	; n,	Tirzepatide 5	mg	<b>•</b> T	irzepa	tide 1	0 mg	Tir.	zepatio	de 15	mg	Tirzepatid	le M	ID
				Сс	opyright	©2024 Eli	Lilly and	Compan	ıy. All righ	ts reserve	d				

Data show the difference in relative to placebo at week from week 36 to 88 for SUR CI, confidence interval; LSM number of participants.



or Interaction nent\*Sex: P<0.001

nent\*Sex: P=0.03

nent\*Sex: P<0.001

nent\*Sex: P<0.001

## Females Receiving Tirzepatide Lost More Weight **Than Males Receiving Tirzepatide**

### Differences in Percent Change in Body Weight for Tirzepatide Treatment Groups

Study	Sex	Treatment	n								V	Veight Loss		Test for li
SURMOUNT-1	Female	Placebo	309							1				Treatment
		Tirzepatide 5 mg	364								-	14.7 (-16.1, -7	13.4)	
		Tirzepatide 10 mg	361							1	-	20.4 (-21.8, -	19.0)	
		Tirzepatide 15 mg	360		H	•				1	-	21.8 (-23.1, -	20.4)	
	Male	Placebo	162							į				
		Tirzepatide 5 mg	175								-	10.9 (-12.6, -9	9.3)	
		Tirzepatide 10 mg	170							i i	-	15.7 (-17.4, -2	14.1)	
		Tirzepatide 15 mg	175			F				i	-	16.5 (-18.1, -2	14.8)	
SURMOUNT-2	Female	Placebo	133											Treatment
		Tirzepatide 10 mg	142								-	11.5 (-13.5, -9	9.6)	
		Tirzepatide 15 mg	133								-	14.1 (-16.1, -1	12.2)	
	Male	Placebo	131											
		Tirzepatide 10 mg	140							i I	-	8.8 (-10.6, -7.	.0)	
		Tirzepatide 15 mg	132							i	-	10.6 (-12.4, -8	8.8)	
SURMOUNT-3	Female	Placebo	127											Treatmen
		Tirzepatide MTD	142							į	-	27.6 (-29.7, -2	25.6)	
	Male	Placebo	75									•		
		Tirzepatide MTD	85								-	18.9 (-21.3, -2	16.4)	
SURMOUNT-4	Female	Placebo	191											Treatment
		Tirzepatide MTD	211								-	23.4 (-25.2, -2	21.7)	
	Male	Placebo	82											
		Tirzepatide MTD	88							i i	-	16.9 (-19.3, -1	14.5)	
weight loss with tirz	epatide			-30	-25	-20	-15	-10	-5	•••••••• 0	 5			
2 for SURMOUNT-	1 to -3 or				LSM	(95%	CI) Ch	ange D	Differer	nce				
AOUNT-4.		Tirzopatida	5 mg	•		·		•			5 ma	Tirzono	ntida N	
, least-squares mea	aii, ii,	<ul> <li>Tirzepatide</li> </ul>	C		-		•		-		Jing			
			(	Jopyrigi	ำเ °∠024 I	=ıı ∟ılıy a	nd Compa	any. All fig	ints reserv	vea				

Data show the difference i relative to placebo at week from week 36 to 88 for SUI CI, confidence interval; LSI number of participants.



Interaction

nt\*Sex: P<0.001

ent\*Sex: P=0.03

nt\*Sex: P<0.001

nt\*Sex: P<0.001

## Females Receiving Tirzepatide Lost More Weight **Than Males Receiving Tirzepatide**

### Differences in Percent Change in Body Weight for Tirzepatide Treatment Groups

	• • • • •		3
Study	Sex	Treatment	n
SURMOUNT-1	Female	Placebo	30
		Tirzepatide 5 mg	36
		Tirzepatide 10 mg	36
		Tirzepatide 15 mg	36
	Male	Placebo	16
		Tirzepatide 5 mg	17
		Tirzepatide 10 mg	17
		Tirzepatide 15 mg	17
SURMOUNT-2	Female	Placebo	13
		Tirzepatide 10 mg	14:
		Tirzepatide 15 mg	13
	Male	Placebo	13
		Tirzepatide 10 mg	14
		Tirzepatide 15 mg	13
SURMOUNT-3	Female	Placebo	12 <sup>-</sup>
		Tirzepatide MTD	14:
	Male	Placebo	7
		Tirzepatide MTD	8
SURMOUNT-4	Female	Placebo	19
		Tirzepatide MTD	21
	Male	Placebo	82
		Tirzepatide MTD	8

Data show the difference in weight loss with tirzepatide relative to placebo at week 72 for SURMOUNT-1 to -3 or from week 36 to 88 for SURMOUNT-4. CI, confidence interval; LSM, least-squares mean; n, number of participants.

Tirzepatide 5 mg





**Test for Interaction** Treatment\*Sex: P<0.001

*Treatment\*Sex: P=0.03* 

Treatment\*Sex: P<0.001

Treatment\*Sex: P<0.001

## Nausea and Vomiting Were Consistently Reported More Frequently in Females than Males

## **Adverse Reactions**

FEMALES	Pla	cebo, % o	f Participa	nts	Tirzepatide (Pooled), % of Participants				
<b>Preferred Term</b>			SM-3 (n=183)		SM-1 (n=1278)				
Nausea	11.7	6.3	18.6	3.8	35.5	27.1	47.5	9.3	

MALES	Placebo, % of Participants				Tirzepatide (Pooled), % of Participants				
<b>Preferred Term</b>		SM-2 (n=156)	SM-3 (n=109)	SM-4 (n=98)	SM-1 (n=618)		SM-3 (n=106)	SM-4* (n=99)	
Nausea	4.8	6.4	6.4	0	17.5	14.7	26.4	5.1	

\*SURMOUNT-4 included a 36-week open label period of TZP treatment. Participants entering the double-blind period were already established on maximum tolerated dose of TZP. Gastrointestinal events occurred more frequently during the dose-escalation phase of the open-label period and hence were not captured as frequently after week 36.



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### Nausea

## Nausea and Vomiting Were Consistently Reported More Frequently in Females than Males

## **Adverse Reactions**

FEMALES	Pla	cebo, % o	f Participa	nts	Tirzepatide (Pooled), % of Participants					
Preferred Term	SM-1	SM-2	SM-3	SM-4	SM-1	SM-2	SM-3	SM-4*		
	(n=436)	(n=159)	(n=183)	(n=237)	(n=1278)	(n=317)	(n=181)	(n=236)		
Nausea	11.7	6.3	18.6	3.8	35.5	27.1	47.5	9.3		
Diarrhea	8.3	9.4	13.1	4.6	21.9	19.6	30.4	11.0		
Constipation	6.9	3.8	9.8	2.5	16.8	8.8	24.9	3.8		
Vomiting	2.3	4.4	1.6	1.7	12.5	15.1	22.7	5.5		
Dyspepsia	5.3	4.4	4.4	0	10.9	8.2	9.9	0.4		
Decreased appetite	3.4	3.1	4.9	0.4	10.7	8.5	10.5	2.1		

MALES	Placebo, % of Participants				Tirzepatide (Pooled), % of Participants			
Preferred Term	SM-1	SM-2	SM-3	SM-4	SM-1	SM-2	SM-3	SM-4*
	(n=207)	(n=156)	(n=109)	(n=98)	(n=618)	(n=306)	(n=106)	(n=99)
Nausea	4.8	6.4	6.4	0	17.5	14.7	26.4	5.1
Diarrhea	5.3	8.3	2.8	5.1	19.1	21.9	32.1	10.1
Constipation	3.4	4.5	1.8	2.0	12.0	8.2	19.8	3.0
Vomiting	0.5	1.9	0.9	0	6.0	8.8	10.4	6.1
Dyspepsia	1.9	1.9	0.9	1.0	8.1	6.2	8.5	0
Decreased appetite	2.9	1.3	2.8	3.1	7.9	11.1	7.5	2.0

\*SURMOUNT-4 included a 36-week open label period of TZP treatment. Participants entering the double-blind period were already established on maximum tolerated dose of TZP. Gastrointestinal events occurred more frequently during the dose-escalation phase of the open-label period and hence were not captured as frequently after week 36.





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### Nausea

### Vomiting

## Conclusion

- In this exploratory analysis, all tirzepatide doses were associated with a significant reduction in body weight in both males and females in comparison to placebo
- A higher proportion of females and males achieved weight reduction thresholds with tirzepatide versus placebo
- Body weight reduction was associated with sex, and tirzepatide was associated with greater weight reduction in females than in males

### **Individual QR Code**



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