

Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Eloralintide and Tirzepatide Co-administered as Once-Weekly Subcutaneous Injections

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PRESENTER DISCLOSURE
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BACKGROUND AND OBJECTIVE

Background

- Eloralintide (LY3841136) is an investigational, **selective, long-acting amylin-1 receptor agonist** under development as a once-weekly treatment for obesity,¹ obstructive sleep apnoea² and knee osteoarthritis pain³
 - In contrast to other amylin receptor agonists in clinical development, eloralintide has a distinct selectivity profile, characterised by strong selectivity for the amylin 1 receptor^{1,4}
 - Eloralintide monotherapy has demonstrated dose-dependent weight reductions of up to 20% after 48 weeks, with good tolerability in Phase 1 and 2 trials, and is in Phase 3 trials for obesity^{1,5-7}
- Tirzepatide is a long-acting dual glucose-dependent insulinotropic polypeptide/glucagon-like peptide-1 receptor agonist, approved for type 2 diabetes, weight management and reduction of cardiovascular risk⁸

Objective

- To assess the safety, pharmacodynamics and pharmacokinetics (PK) of tirzepatide and eloralintide, alone and in combination, in adults with obesity or overweight, without type 2 diabetes

1. Bhattachar S, et al. *Diabetes Obes Metab*. 2026;28:2651-2660. 2. NCT07369011. 3. NCT07353931. 4. Briere DA, et al. *Mol Metab*. 2025;102:102271. 5. Billings LK, et al. *Lancet*. 2025;406:2631-2643.

6. NCT07321886. 7. NCT07282600. 8. Mounjaro (tirzepatide) [summary of product characteristics]. Utrecht, the Netherlands: Eli Lilly Nederland B.V., 2026.

Two Phase 1b Studies of Combined Eloralintide and Tirzepatide in Adults With Obesity/Overweight, Without Type 2 Diabetes

Studies

- **Study #1:** High-dose combination treatment
 - Japan study: Titrated eloralintide 9 mg and tirzepatide 15 mg in combination vs. each alone, or placebo
- **Study #2:** Different dose levels and dose combinations of eloralintide and tirzepatide
 - US study:
 - Group 1: Low-dose combination treatment – un-titrated eloralintide (3, 6 or 9 mg) and tirzepatide vs. tirzepatide alone
 - Group 2: High-dose combination treatment – titrated eloralintide 9 mg and tirzepatide 15 mg vs. tirzepatide 15 mg alone

Endpoints

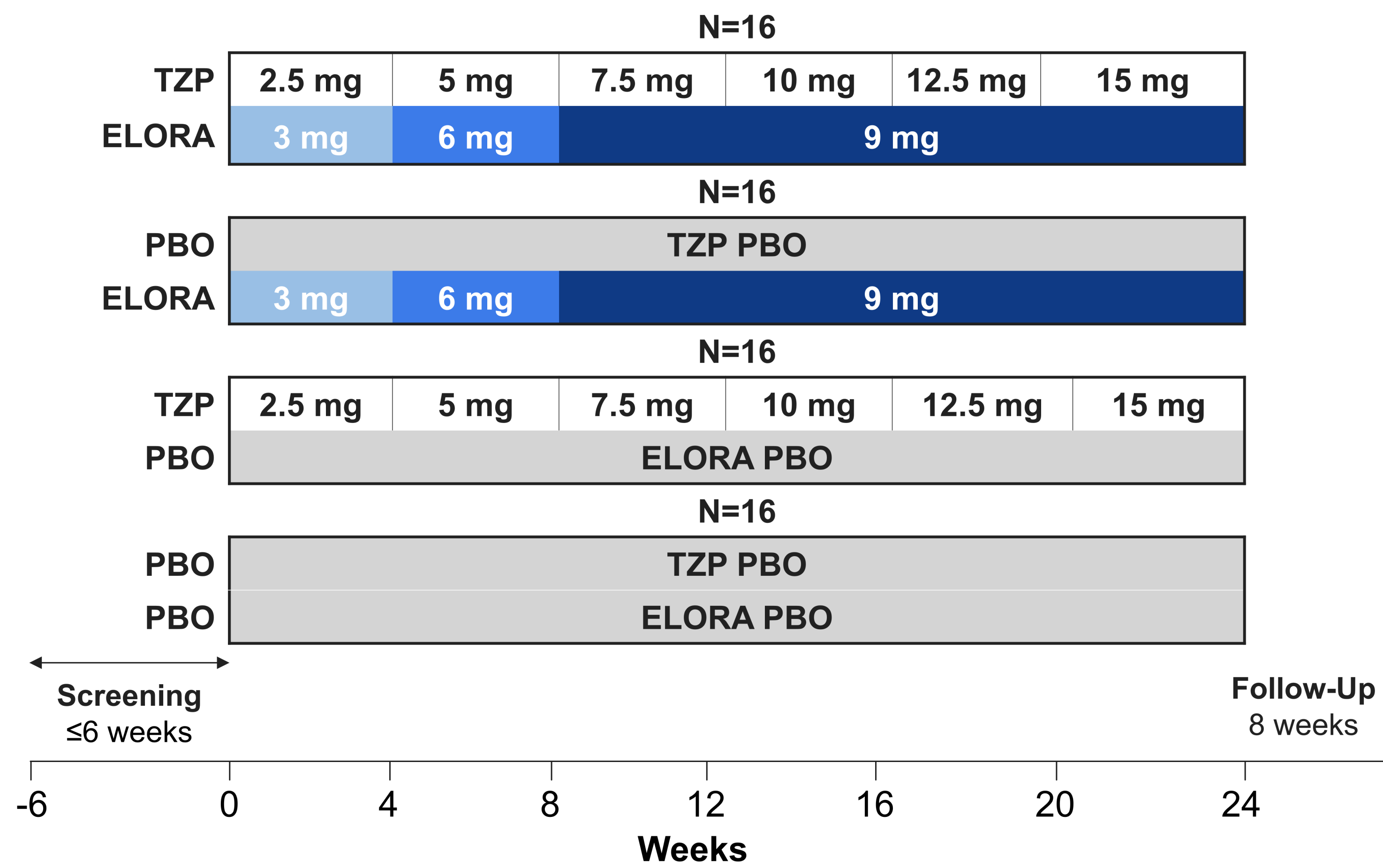
- **Primary Endpoints** (Safety and Tolerability)
 - Incidence of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs)
- **Secondary Endpoints**
 - Percent change in body weight from baseline^a
 - Eloralintide PK measures, including area under the concentration-time curve (AUC) and maximum observed drug concentration in plasma ($C_{\max}$)

^aFor Study #2, results are presented for the last on-treatment (final dosing) visit time point. Treatment was started at Week 0, with the final dose being administered on Weeks 15 and 31 for Groups 1 and 2, respectively.
PK=pharmacokinetic.

Study #1: Study Design and Baseline Characteristics

Investigator- and participant-blinded, randomised, placebo-controlled trial in adults with obesity/overweight, without type 2 diabetes, with stable body weight; **BMI 27-40 kg/m²**

Titrated Eloralintide (ELORA) 9 mg + Tirzepatide (TZP) 15 mg



Baseline Characteristic	PBO	TZP 2.5→15 PBO	ELORA 3→9 PBO	ELORA 3→9 TZP 2.5→15
N	16	16	16	16
Age (SD), years	40.1 (10.9)	41.4 (12.7)	46.1 (11.1)	41.8 (10.3)
Female, n (%)	3 (18.8)	5 (31.3)	4 (25.0)	4 (25.0)
Weight (SD), kg	88.4 (10.7)	84.0 (15.6)	87.7 (10.8)	86.6 (12.9)
BMI (SD), kg/m ²	30.8 (2.7)	29.8 (3.0)	30.3 (2.5)	30.9 (3.0)

Notes: All doses are mg. Mean values presented for age, weight and BMI.

- Participants were randomised 1:1:1:1 to receive PBO, tirzepatide+PBO, eloralintide+PBO or eloralintide+tirzepatide
- No statistically significant differences in baseline features across treatment arms

Note: Blinded tirzepatide and eloralintide or matched PBO were administered subcutaneously once weekly. BMI=body mass index; PBO=placebo; SD=standard deviation.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Eloralintide or Tirzepatide Alone (Study #1)

Summary of Overall Safety and AEs of Special Interest

No. of Participants With AEs, n (%)	PBO	TZP 2.5→15 ^a PBO	ELORA 3→9 PBO
N	16	16	16
All TEAEs	8 (50.0)	12 (75.0)	12 (75.0)
Mild	8 (50.0)	12 (75.0)	12 (75.0)
Moderate	1 (6.3)	1 (6.3)	2 (12.5)
Severe	0	0	0
Leading to study discontinuation	0	0	0
Serious AEs	0	0	1 (6.3)
Treatment-related AEs	5 (31.3)	9 (56.3)	10 (62.5)
GI AEs	3 (18.8)	6 (37.5)	3 (18.8)
Decreased appetite	2 (12.5)	6 (37.5)	9 (56.3)
Nausea	0	3 (18.8)	0
Constipation	2 (12.5)	2 (12.5)	0
Vomiting	0	3 (18.8)	0
Dyspepsia	0	0	0
Diarrhoea	0	2 (12.5)	2 (12.5)
Injection site reactions	0	4 (25.0)	1 (6.3)
Fatigue	0	0	0

■ Tirzepatide GI AEs were consistent with previous studies¹

^aTirzepatide dose reductions were permitted as necessary; for 4 participants, the tirzepatide dose was reduced to 5 mg at Week 8 or after.
Note: All doses are mg.
¹. Rubino DM, et al. *Diabetes Obes Metab.* 2025;27:1826-1835. ². Billings LK, et al. *Lancet.* 2025;406:2631-2643. ³. NCT06230523.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZP=tirzepatide.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Eloralintide or Tirzepatide Alone (Study #1)

Summary of Overall Safety and AEs of Special Interest

No. of Participants With AEs, n (%)	PBO	TZP 2.5→15 ^a PBO	ELORA 3→9 PBO
N	16	16	16
All TEAEs	8 (50.0)	12 (75.0)	12 (75.0)
Mild	8 (50.0)	12 (75.0)	12 (75.0)
Moderate	1 (6.3)	1 (6.3)	2 (12.5)
Severe	0	0	0
Leading to study discontinuation	0	0	0
Serious AEs	0	0	1 (6.3)
Treatment-related AEs	5 (31.3)	9 (56.3)	10 (62.5)
GI AEs	3 (18.8)	6 (37.5)	3 (18.8)
Decreased appetite	2 (12.5)	6 (37.5)	9 (56.3)
Nausea	0	3 (18.8)	0
Constipation	2 (12.5)	2 (12.5)	0
Vomiting	0	3 (18.8)	0
Dyspepsia	0	0	0
Diarrhoea	0	2 (12.5)	2 (12.5)
Injection site reactions	0	4 (25.0)	1 (6.3)
Fatigue	0	0	0

- Tirzepatide GI AEs were consistent with previous studies¹
- Eloralintide alone had placebo-like GI tolerability as previously demonstrated^{2,3}

^aTirzepatide dose reductions were permitted as necessary; for 4 participants, the tirzepatide dose was reduced to 5 mg at Week 8 or after.
Note: All doses are mg.
¹. Rubino DM, et al. *Diabetes Obes Metab.* 2025;27:1826-1835. ². Billings LK, et al. *Lancet.* 2025;406:2631-2643. ³. NCT06230523.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZP=tirzepatide.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Eloralintide or Tirzepatide Alone (Study #1)

Summary of Overall Safety and AEs of Special Interest

No. of Participants With AEs, n (%)	PBO	TZP 2.5→15 ^a PBO	ELORA 3→9 PBO	ELORA 3→9 TZP 2.5→15 ^a
N	16	16	16	16
All TEAEs	8 (50.0)	12 (75.0)	12 (75.0)	14 (87.5)
Mild	8 (50.0)	12 (75.0)	12 (75.0)	13 (81.3)
Moderate	1 (6.3)	1 (6.3)	2 (12.5)	6 (37.5)
Severe	0	0	0	0
Leading to study discontinuation	0	0	0	2 (12.5)
Serious AEs	0	0	1 (6.3)	0
Treatment-related AEs	5 (31.3)	9 (56.3)	10 (62.5)	14 (87.5)
GI AEs	3 (18.8)	6 (37.5)	3 (18.8)	10 (62.5)
Decreased appetite	2 (12.5)	6 (37.5)	9 (56.3)	10 (62.5)
Nausea	0	3 (18.8)	0	4 (25.0)
Constipation	2 (12.5)	2 (12.5)	0	4 (25.0)
Vomiting	0	3 (18.8)	0	3 (18.8)
Dyspepsia	0	0	0	0
Diarrhoea	0	2 (12.5)	2 (12.5)	4 (25.0)
Injection site reactions	0	4 (25.0)	1 (6.3)	4 (25.0)
Fatigue	0	0	0	0

- Tirzepatide GI AEs were consistent with previous studies¹
- Eloralintide alone had placebo-like GI tolerability as previously demonstrated^{2,3}
- Combined treatment arm had higher rates of TEAEs compared with eloralintide or tirzepatide, alone, or PBO

^aTirzepatide dose reductions were permitted as necessary; for 4 participants, the tirzepatide dose was reduced to 5 mg at Week 8 or after.
Note: All doses are mg.
¹. Rubino DM, et al. *Diabetes Obes Metab*. 2025;27:1826-1835. ². Billings LK, et al. *Lancet*. 2025;406:2631-2643. ³. NCT06230523.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZP=tirzepatide.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Eloralintide or Tirzepatide Alone (Study #1)

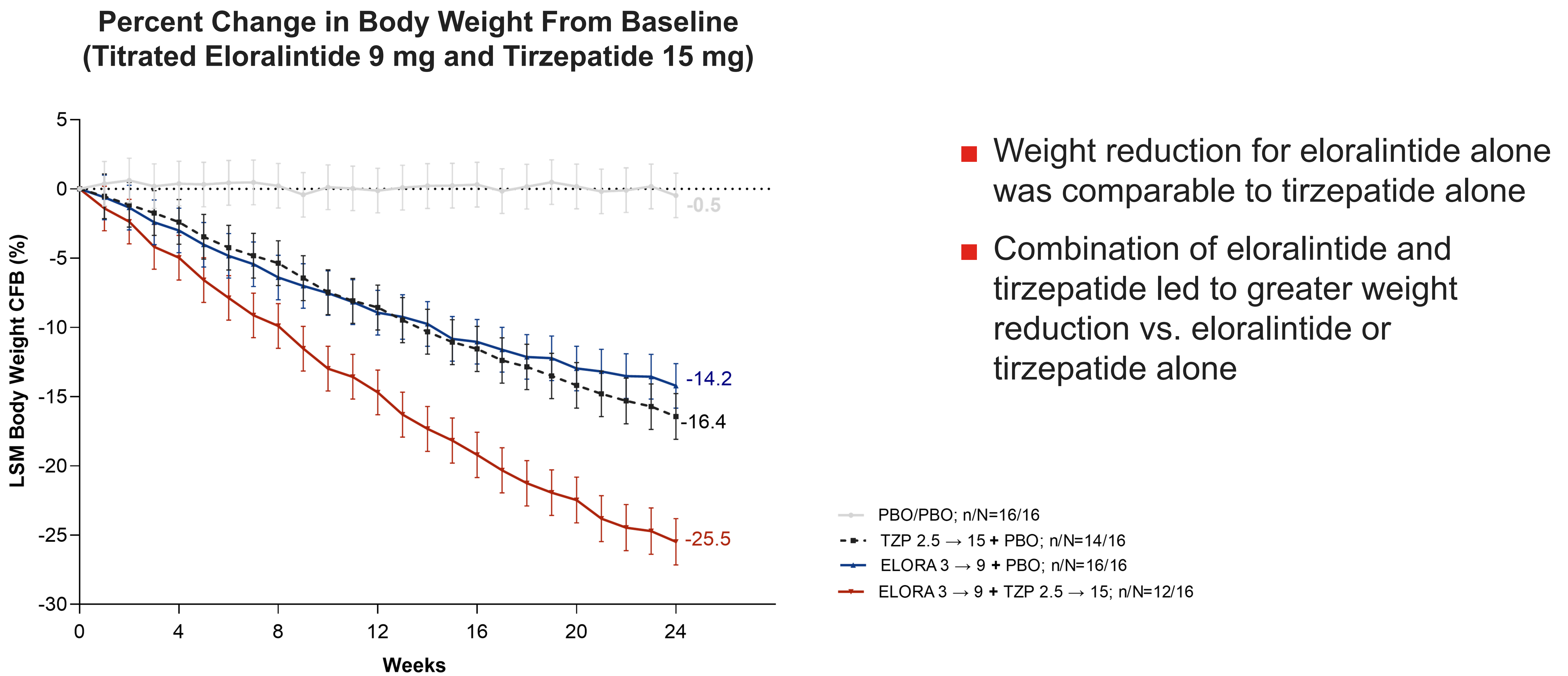
Summary of Overall Safety and AEs of Special Interest

No. of Participants With AEs, n (%)	PBO	TZP 2.5→15 ^a PBO	ELORA 3→9 PBO	ELORA 3→9 TZP 2.5→15 ^a
N	16	16	16	16
All TEAEs	8 (50.0)	12 (75.0)	12 (75.0)	14 (87.5)
Mild	8 (50.0)	12 (75.0)	12 (75.0)	13 (81.3)
Moderate	1 (6.3)	1 (6.3)	2 (12.5)	6 (37.5)
Severe	0	0	0	0
Leading to study discontinuation	0	0	0	2 (12.5)
Serious AEs	0	0	1 (6.3)	0
Treatment-related AEs	5 (31.3)	9 (56.3)	10 (62.5)	14 (87.5)
GI AEs	3 (18.8)	6 (37.5)	3 (18.8)	10 (62.5)
Decreased appetite	2 (12.5)	6 (37.5)	9 (56.3)	10 (62.5)
Nausea	0	3 (18.8)	0	4 (25.0)
Constipation	2 (12.5)	2 (12.5)	0	4 (25.0)
Vomiting	0	3 (18.8)	0	3 (18.8)
Dyspepsia	0	0	0	0
Diarrhoea	0	2 (12.5)	2 (12.5)	4 (25.0)
Injection site reactions	0	4 (25.0)	1 (6.3)	4 (25.0)
Fatigue	0	0	0	0

- Tirzepatide GI AEs were consistent with previous studies¹
- Eloralintide alone had placebo-like GI tolerability as previously demonstrated^{2,3}
- Combined treatment arm had higher rates of TEAEs compared with eloralintide or tirzepatide, alone, or PBO
- The most common AEs were GI AEs
- There were no deaths

^aTirzepatide dose reductions were permitted as necessary; for 4 participants, the tirzepatide dose was reduced to 5 mg at Week 8 or after.
Note: All doses are mg.
¹. Rubino DM, et al. *Diabetes Obes Metab.* 2025;27:1826-1835. ². Billings LK, et al. *Lancet.* 2025;406:2631-2643. ³. NCT06230523.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZP=tirzepatide.

Combination Treatment Resulted in Greater Weight Reduction vs. Eloralintide or Tirzepatide Alone (Study #1)



Notes: All doses are mg. Data are modeled LSM (90% CI). Baseline was defined as the last scheduled value recorded before the first dose.
CFB=change from baseline; CI=confidence interval; ELORA=eloralintide; LSM=least squares mean; N=overall number of participants in treatment arm; n=number of participants with data at final endpoint shown; PBO=placebo; TZP=tirzepatide.

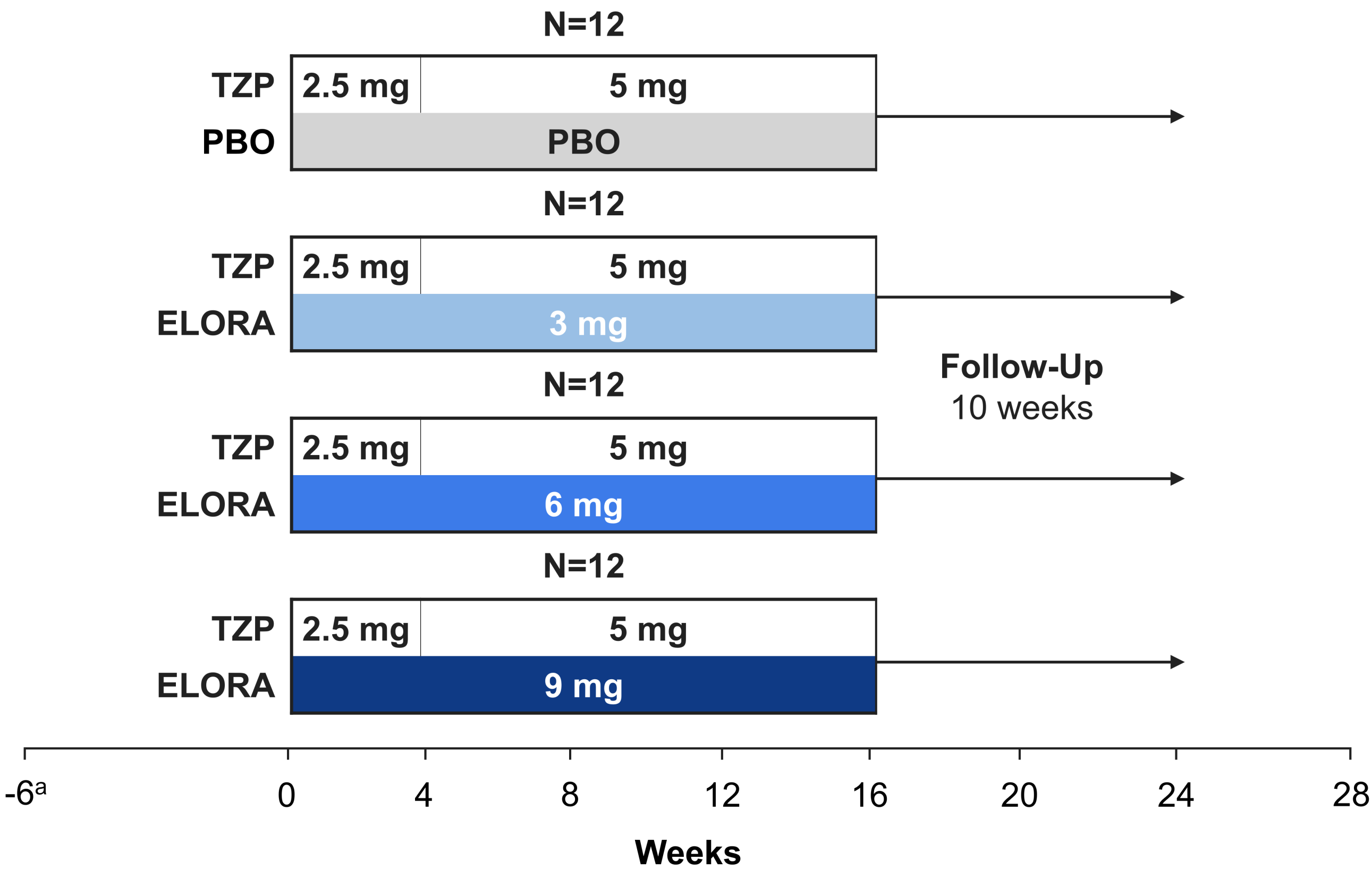
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Study #2: Study Design and Baseline Characteristics

Low-Dose Combination (Group 1)

Investigator- and participant-blinded, randomised, placebo-controlled trial in adults with obesity/overweight, without type 2 diabetes, with stable body weight; **BMI 27-45 kg/m²**

Group 1
Un-titrated ELORA and TZP 5 mg



Baseline Characteristic	Pooled PBO TZP 2.5→5	ELORA 3 TZP 2.5→5	ELORA 6 TZP 2.5→5	ELORA 9 TZP 2.5→5
N	12	12	12	12
Age (SD), years	50.3 (14.2)	41.5 (13.8)	42.4 (7.0)	41.0 (11.1)
Female, n (%)	7 (58.3)	7 (58.3)	8 (66.7)	8 (66.7)
Weight (SD), kg	94.8 (17.1)	86.9 (7.5)	97.9 (18.4)	89.9 (9.6)
BMI (SD), kg/m ²	33.2 (5.2)	32.3 (3.2)	33.1 (4.4)	31.8 (2.2)

Notes: All doses are mg. Mean values presented for age, weight and BMI.

- Randomisation: 16 participants in each cohort group were randomised 3:1 to receive eloralintide+tirzepatide (N=12) or tirzepatide+PBO (N=4)
- No clinically important differences in baseline features between study groups

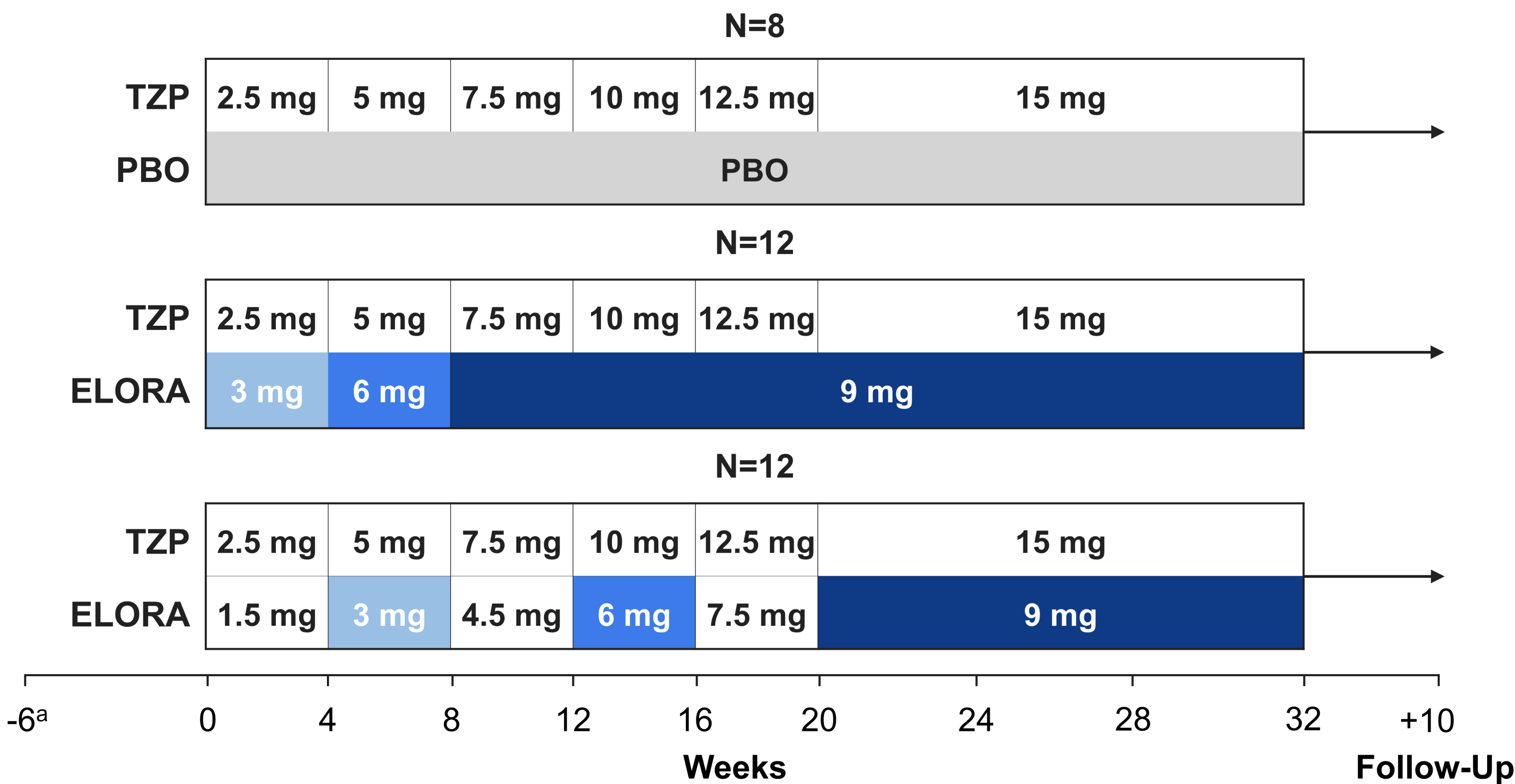
^aScreening ≤6 weeks.
Note: Tirzepatide was administered as open-label; blinded eloralintide or matched PBO were administered subcutaneously once weekly.
BMI=body mass index; ELORA=eloralintide; PBO=placebo; SD=standard deviation; TZP=tirzepatide.

Study #2: Study Design and Baseline Characteristics

High-Dose Combination (Group 2)

Investigator- and participant-blinded, randomised, placebo-controlled trial in adults with obesity/overweight, without type 2 diabetes, with stable body weight; **BMI 27-45 kg/m²**

Group 2 Titrated ELORA and TZP 15 mg



Baseline Characteristic	Pooled PBO TZP 2.5→15	ELORA 1.5→9 TZP 2.5→15	ELORA 3→9 TZP 2.5→15
N	8	12	12
Age (SD), years	43.5 (13.9)	45.8 (11.2)	45.4 (10.1)
Female, n (%)	6 (75.0)	8 (66.7)	6 (50.0)
Weight (SD), kg	92.2 (16.4)	93.2 (18.2)	102.3 (15.0)
BMI (SD), kg/m ²	33.8 (3.2)	32.2 (4.1)	33.8 (4.3)

Notes: All doses are mg. Mean values presented for age, weight and BMI.

- Randomisation: 16 participants in each cohort group were randomised 3:1 to receive eloralintide+tirzepatide (N=12) or tirzepatide+PBO (N=4)
- No clinically important differences in baseline demographics and characteristics between study groups

^aScreening ≤6 weeks.
Note: Tirzepatide was administered as open-label; blinded eloralintide or matched PBO were administered subcutaneously once weekly.
BMI=body mass index; ELORA=eloralintide; PBO=placebo; SD=standard deviation; TZP=tirzepatide.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Tirzepatide 5 mg Alone (Study #2): Low-Dose Combination

Summary of Overall Safety and AEs of Special Interest
Group 1: Un-titrated ELORA + TZP 5

No. of Participants With AEs, n (%)	PBO TZP 2.5→5	ELORA 3 TZP 2.5→5	ELORA 6 TZP 2.5→5	ELORA 9 TZP 2.5→5
N	12	12	12	12
All TEAEs	10 (83.3)	11 (91.7)	11 (91.7)	12 (100)
Mild	9 (75.0)	11 (91.7)	11 (91.7)	12 (100)
Moderate	1 (8.3)	2 (16.7)	4 (33.3)	2 (16.7)
Severe	0	0	1 (8.3)	0
Leading to study discontinuation	0	0	1 (8.3)	2 (16.7)
Serious AEs	0	0	1 (8.3)	0
Treatment-related AEs	9 (75.0)	9 (75.0)	10 (83.3)	12 (100)
GI AEs	6 (50.0)	7 (58.3)	8 (66.7)	9 (75.0)
Decreased appetite	4 (33.3)	4 (33.3)	3 (25.0)	9 (75.0)
Nausea	2 (16.7)	4 (33.3)	4 (33.3)	8 (66.7)
Constipation	0	2 (16.7)	3 (25.0)	2 (16.7)
Vomiting	0	1 (8.3)	4 (33.3)	3 (25.0)
Dyspepsia	1 (8.3)	2 (16.7)	3 (25.0)	0
Diarrhoea	5 (41.7)	3 (25.0)	1 (8.3)	0
Injection site reactions	1 (8.3)	0	0	4 (33.3)
Fatigue	0	3 (25.0)	2 (16.7)	2 (16.7)

- AEs with tirzepatide were consistent with previous studies¹
- Combined treatment arms had higher rates of TEAEs compared with tirzepatide alone

Note: All doses are mg.
¹. Rubino DM, et al. *Diabetes Obes Metab.* 2025;27:1826-1835.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZP=tirzepatide.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Tirzepatide 5 mg Alone (Study #2): Low-Dose Combination

Summary of Overall Safety and AEs of Special Interest
Group 1: Un-titrated ELORA + TZIP 5

No. of Participants With AEs, n (%)	PBO TZP 2.5→5	ELORA 3 TZP 2.5→5	ELORA 6 TZP 2.5→5	ELORA 9 TZP 2.5→5
N	12	12	12	12
All TEAEs	10 (83.3)	11 (91.7)	11 (91.7)	12 (100)
Mild	9 (75.0)	11 (91.7)	11 (91.7)	12 (100)
Moderate	1 (8.3)	2 (16.7)	4 (33.3)	2 (16.7)
Severe	0	0	1 (8.3)	0
Leading to study discontinuation	0	0	1 (8.3)	2 (16.7)
Serious AEs	0	0	1 (8.3)	0
Treatment-related AEs	9 (75.0)	9 (75.0)	10 (83.3)	12 (100)
GI AEs	6 (50.0)	7 (58.3)	8 (66.7)	9 (75.0)
Decreased appetite	4 (33.3)	4 (33.3)	3 (25.0)	9 (75.0)
Nausea	2 (16.7)	4 (33.3)	4 (33.3)	8 (66.7)
Constipation	0	2 (16.7)	3 (25.0)	2 (16.7)
Vomiting	0	1 (8.3)	4 (33.3)	3 (25.0)
Dyspepsia	1 (8.3)	2 (16.7)	3 (25.0)	0
Diarrhoea	5 (41.7)	3 (25.0)	1 (8.3)	0
Injection site reactions	1 (8.3)	0	0	4 (33.3)
Fatigue	0	3 (25.0)	2 (16.7)	2 (16.7)

- AEs with tirzepatide were consistent with previous studies¹
- Combined treatment arms had higher rates of TEAEs compared with tirzepatide alone
- The most common AEs were GI AEs
- There were no deaths

Note: All doses are mg.
¹ Rubino DM, et al. *Diabetes Obes Metab.* 2025;27:1826-1835.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZP=tirzepatide.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Tirzepatide 15 mg Alone (Study #2): High-Dose Combination

Summary of Overall Safety and AEs of Special Interest
Group 2: Titrated ELORA + TZP 15

No. of Participants With AEs, n (%)	PBO TZP 2.5→15	ELORA 1.5→9 ^a TZP 2.5→15	ELORA 3→9 TZP 2.5→15
N	8	12	12
All TEAEs	6 (75.0)	12 (100)	10 (83.3)
Mild	6 (75.0)	11 (91.7)	9 (75.0)
Moderate	2 (25.0)	10 (83.3)	5 (41.7)
Severe	0	1 (8.3)	0
Leading to study discontinuation	1 (12.5)	4 (33.3)	6 (50.0)
Serious AEs	0	1 (8.3)	3 (25.0)
Treatment-related AEs	5 (62.5)	11 (91.7)	10 (83.3)
GI AEs	4 (50.0)	11 (91.7)	6 (50.0)
Decreased appetite	2 (25.0)	7 (58.3)	1 (8.3)
Nausea	2 (25.0)	8 (66.7)	6 (50.0)
Constipation	3 (37.5)	5 (41.7)	2 (16.7)
Vomiting	1 (12.5)	4 (33.3)	4 (33.3)
Dyspepsia	3 (37.5)	2 (16.7)	1 (8.3)
Diarrhoea	1 (12.5)	4 (33.3)	1 (8.3)
Injection site reactions	0	0	0
Fatigue	2 (25.0)	5 (41.7)	0

- AEs with tirzepatide were consistent with previous studies¹
- Combined treatment arms had higher rates of TEAEs compared with tirzepatide alone

^aDose reductions were allowed to improve participant retention, resulting in a greater number of completers vs. other combined treatment arm, although several completers did not reach the highest target doses.
Note: All doses are mg. 1. Rubino DM, et al. *Diabetes Obes Metab.* 2025;27:1826-1835.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZP=tirzepatide.

TEAEs Were More Frequent With Combination Treatment Therapy Than With Tirzepatide 15 mg Alone (Study #2): High-Dose Combination

Summary of Overall Safety and AEs of Special Interest
Group 2: Titrated ELORA + TZIP 15

No. of Participants With AEs, n (%)	PBO TZP 2.5→15	ELORA 1.5→9 ^a TZP 2.5→15	ELORA 3→9 TZP 2.5→15
N	8	12	12
All TEAEs	6 (75.0)	12 (100)	10 (83.3)
Mild	6 (75.0)	11 (91.7)	9 (75.0)
Moderate	2 (25.0)	10 (83.3)	5 (41.7)
Severe	0	1 (8.3)	0
Leading to study discontinuation	1 (12.5)	4 (33.3)	6 (50.0)
Serious AEs	0	1 (8.3)	3 (25.0)
Treatment-related AEs	5 (62.5)	11 (91.7)	10 (83.3)
GI AEs	4 (50.0)	11 (91.7)	6 (50.0)
Decreased appetite	2 (25.0)	7 (58.3)	1 (8.3)
Nausea	2 (25.0)	8 (66.7)	6 (50.0)
Constipation	3 (37.5)	5 (41.7)	2 (16.7)
Vomiting	1 (12.5)	4 (33.3)	4 (33.3)
Dyspepsia	3 (37.5)	2 (16.7)	1 (8.3)
Diarrhoea	1 (12.5)	4 (33.3)	1 (8.3)
Injection site reactions	0	0	0
Fatigue	2 (25.0)	5 (41.7)	0

- AEs with tirzepatide were consistent with previous studies¹
- Combined treatment arms had higher rates of TEAEs compared with tirzepatide alone

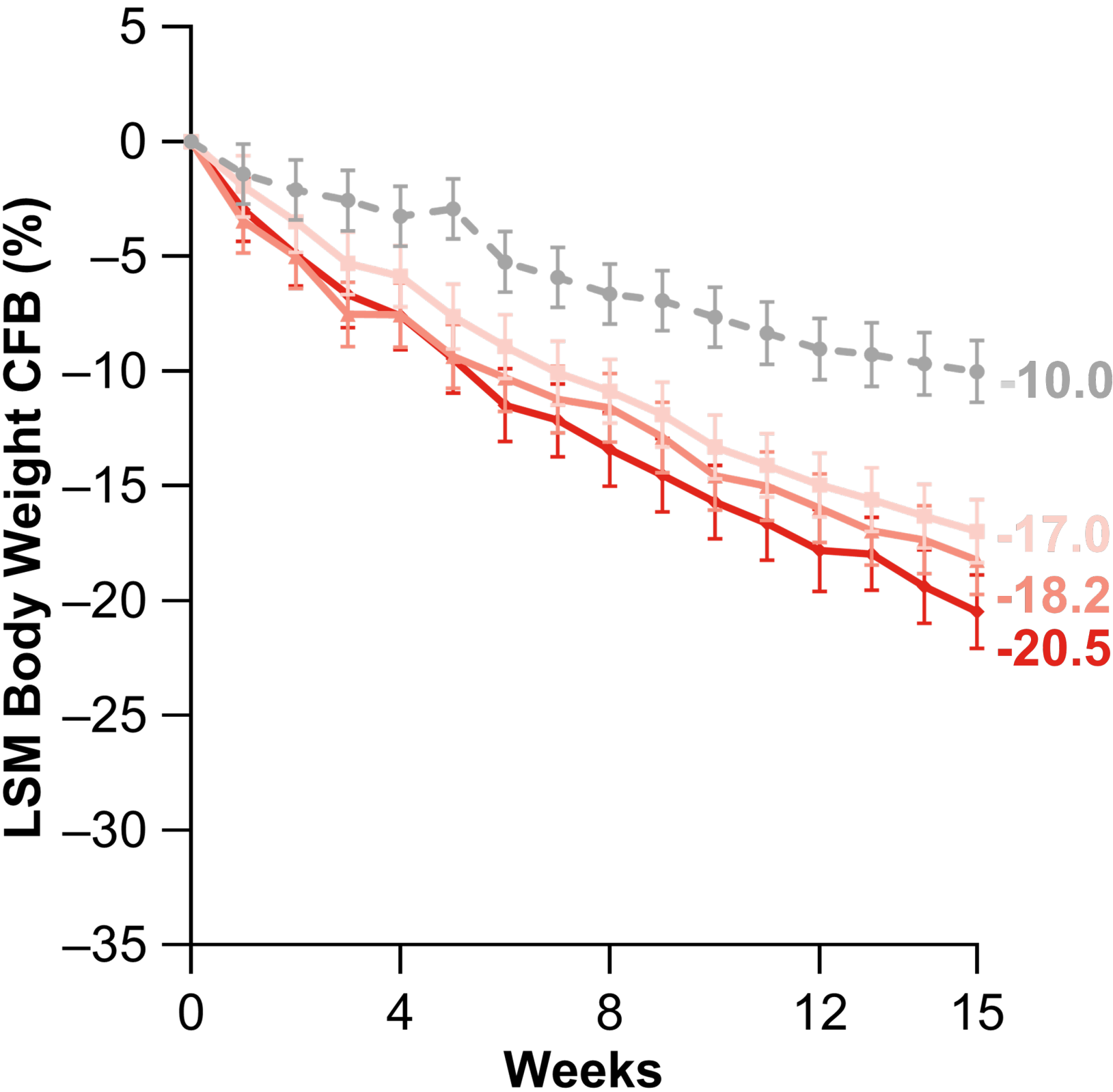
^aDose reductions were allowed to improve participant retention, resulting in a greater number of completers vs. other combined treatment arm, although several completers did not reach the highest target doses.
Note: All doses are mg. 1. Rubino DM, et al. *Diabetes Obes Metab.* 2025;27:1826-1835.
AE=adverse event; ELORA=eloralintide; GI=gastrointestinal; N=number of participants in the population; PBO=placebo; TEAE=treatment-emergent AE; TZIP=tirzepatide.

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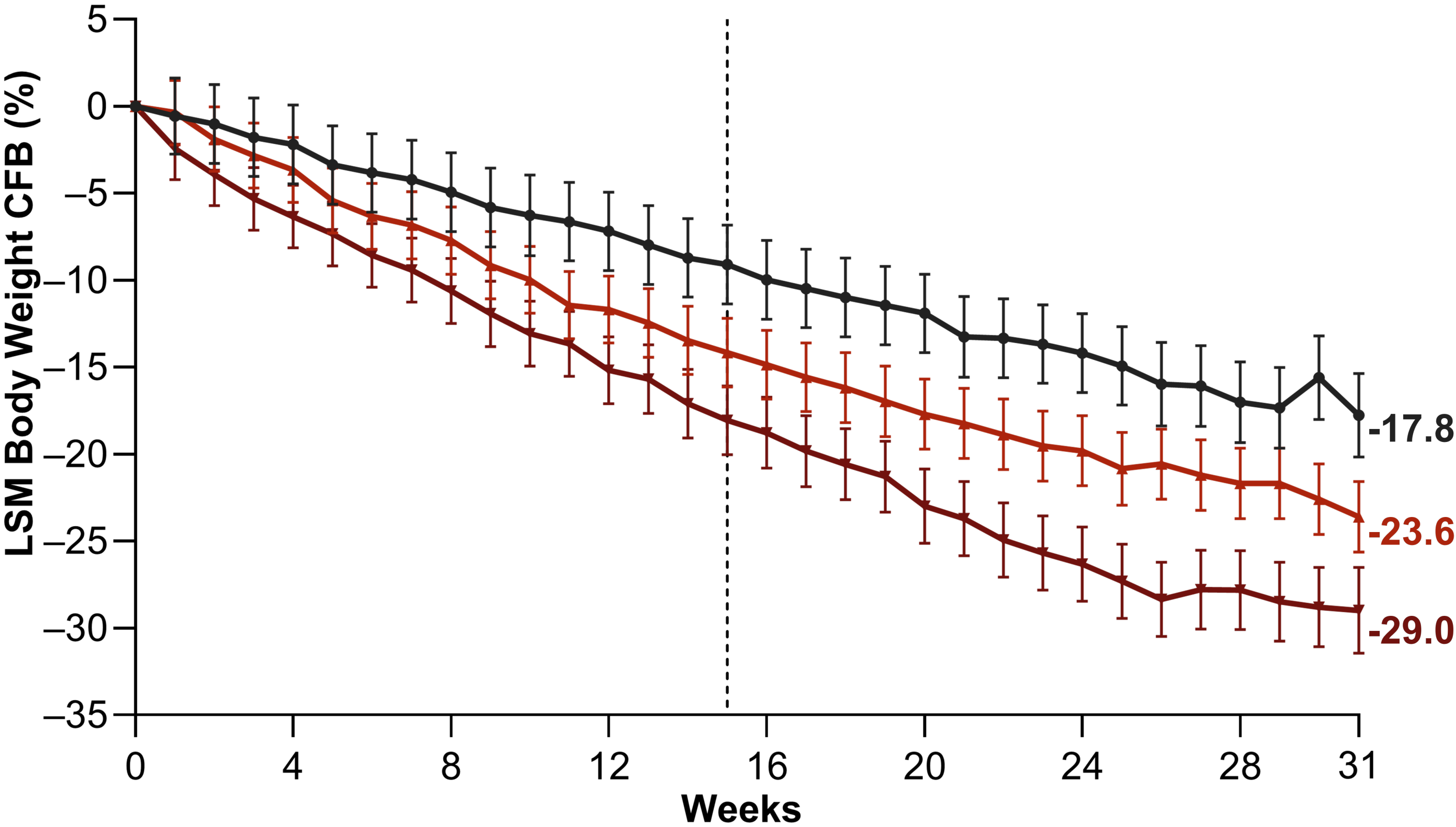
Study #2: Combined Treatment Associated With Greater Weight Reduction vs. Tirzepatide Alone

Percentage Change in Body Weight Over Time

Low-Dose Combination (Group 1)
Un-titrated Eloralintide + Tirzepatide 5 mg
CFB Over 15 Weeks



High-Dose Combination (Group 2)
Titrated Eloralintide + Tirzepatide 15 mg
CFB Over 31 Weeks



Legend:

- Grey dashed line: PBO + TZP 2.5 → 5 (n/N=10/12)
- Light red solid line: ELORA 6 + TZP 2.5 → 5 (n/N=8/12)
- Pink solid line: ELORA 3 + TZP 2.5 → 5 (n/N=10/12)
- Dark red solid line: ELORA 9 + TZP 2.5 → 5 (n/N=6/12)
- Black solid line: PBO + TZP 2.5 → 15 (n/N=5/8)
- Dark red solid line: ELORA 3 → 9 + TZP 2.5 → 15 (n/N=3/12)
- Brown solid line: ELORA 1.5 → 9 + TZP 2.5 → 15 (n/N=7/12)
- Red solid line: ELORA 3 → 9 + TZP 2.5 → 15 (n/N=3/12)

Notes: All doses are mg. Data are modelled LSM (90% CI).
CFB=change from baseline; CI=confidence interval; ELORA=eloralintide; LSM=least squares mean; N=overall number of participants in treatment arm; n=number of participants with data at final endpoint shown;
PBO=placebo; TZP=tirzepatide.

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Study #2: Eloralintide Demonstrated Consistent PK Across Doses and Combinations With Tirzepatide

PK Parameters for Eloralintide Dosed in Combination With Tirzepatide

Parameter	Group 1: Low-Dose Combination Un-titrated ELORA + TZP 5 (16 Weeks)			Group 2: High-Dose Combination Titrated ELORA + TZP 15 (32 Weeks)	
	ELORA 3 mg + TZP 2.5 → 5	ELORA 6 mg + TZP 2.5 → 5	ELORA 9 mg + TZP 2.5 → 5	ELORA 1.5 → 9 + TZP 2.5 → 15	ELORA 3 → 9 + TZP 2.5 → 15
N	10	8	6	3	2
AUC _{(0-168)ss} , ng•h/mL	135,000 (16.0)	236,000 (20.6) ^a	415,000 (14.7)	333,000 (36.5)	NC
C _{max} ss, ng/mL	1010 (19.4)	1730 (18.8)	3270 (13.9)	2750 (21.9)	NC
t _{max} ss, median (range), h	24.0 (24.0-72.2)	24.0 (24.0-72.0)	36.1 (24.0-48.1)	6.0 (6.0-24.0)	NC (24.0-24.0)
t _{1/2} , geometric mean (range), h	235 (202-282)	243 (220-297) ^a	251 (231-304)	235 (192-287)	NC (232-236)

■ Combination did not alter PK of eloralintide

^aN=7. Notes: Data are geometric mean (geometric CV%) unless stated otherwise. PK population was comprised of all participants who received ≥1 dose of the study intervention and had sufficient PK data available for analysis. AUC_{(0-168)ss}=area under the concentration-time curve during 1 dosing interval at steady state; C_{max,ss}=maximum observed drug concentration in plasma at steady state; CV=coefficient of variation; ELORA=eloralintide; N=PK population for treatment arm; NC=not calculated; PK=pharmacokinetic; t_{1/2}=half-life associated with the terminal rate constant in non-compartmental analysis; t_{max,ss}=time to C_{max,ss}; TZP=tirzepatide.

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CONCLUSIONS

- These Phase 1b studies in adults with obesity or overweight, without type 2 diabetes, demonstrated that eloralintide in combination with tirzepatide was generally well tolerated and resulted in meaningful weight reduction that exceeded the effect of tirzepatide alone across all evaluated doses
- Body weight loss
 - In the low-dose cohorts, the combination of un-titrated 3 mg eloralintide with 5 mg tirzepatide achieved 17% body weight loss at Week 15
 - Greater weight loss was achieved at the highest doses of the combination; augmented weight loss up to 29% was achieved at Week 31
- Safety and tolerability were generally aligned with those previously seen with tirzepatide and eloralintide, alone¹⁻³
 - GI AEs (nausea, vomiting and diarrhoea) were generally more frequent in combination arms compared with tirzepatide alone, and were generally mild to moderate in severity
- PK of eloralintide in combination arms was similar to eloralintide alone^{4,5}
- A Phase 2 study examining eloralintide alone or in combination with tirzepatide in participants with obesity and type 2 diabetes (NCT06603571) will be presented later today

1. Billings LK, et al. *Lancet*. 2025;406:2631-2643. 2. NCT06230523. 3. Rubino DM, et al. *Diabetes Obes Metab*. 2025;27:1826-1835. 4. Bhattachar S, et al. *Diabetes Obes Metab*. 2026;28:2651-2660.

5. Briere DA, et al. *Mol Metab*. 2025;102:102271.

AE=adverse event; GI=gastrointestinal; PK=pharmacokinetics.

Disclosures

- **S. Bhattachar, R. Taylor, K. Takenouchi, R. Nasu, L. S. Tham, S. Bhamidipaty-Pelosi, K. Ohwaki, E. J. Pratt and K. J. Mather** are full-time employees and shareholders of: Eli Lilly and Company
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