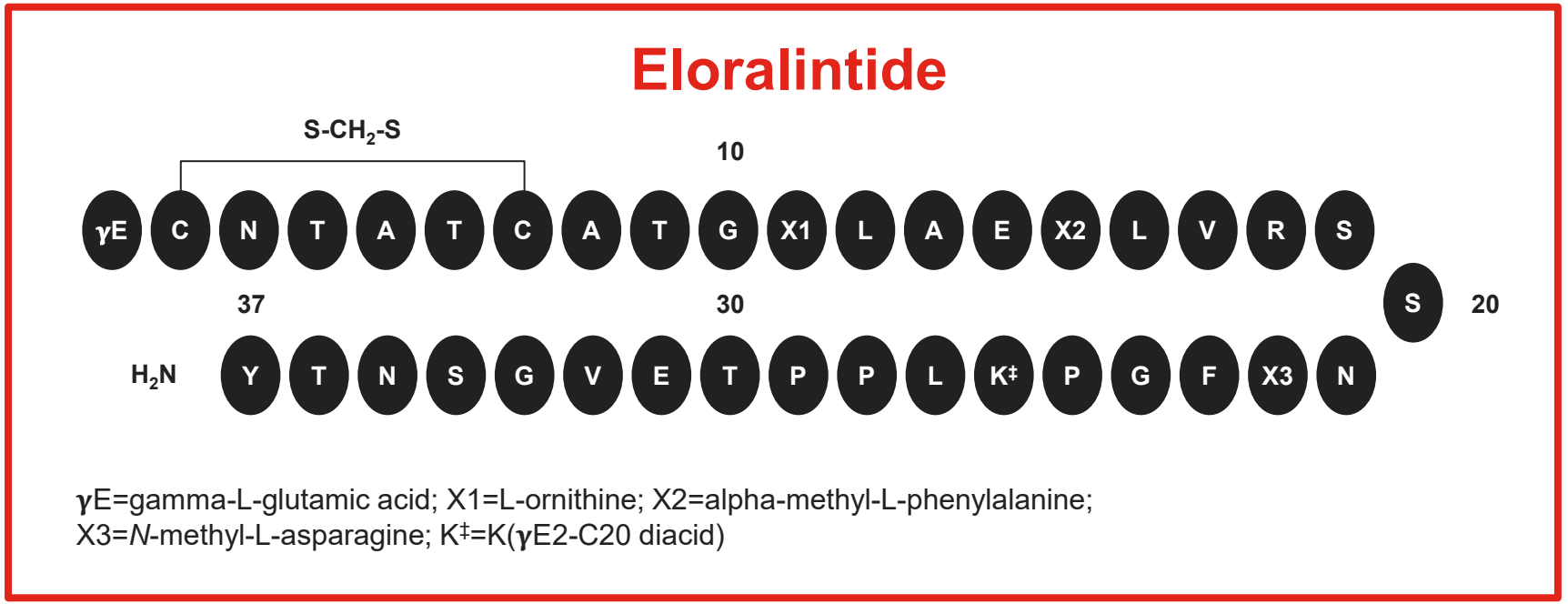
Eloralintide Phase 2 Study in Adult Participants With Overweight or Obesity: Design and Study Population

Stanley Hsia, MD

Obesity Week 2025; Atlanta, GA; November 4-7, 2025

Sponsored by Eli Lilly and Company

Introduction to Eloralintide

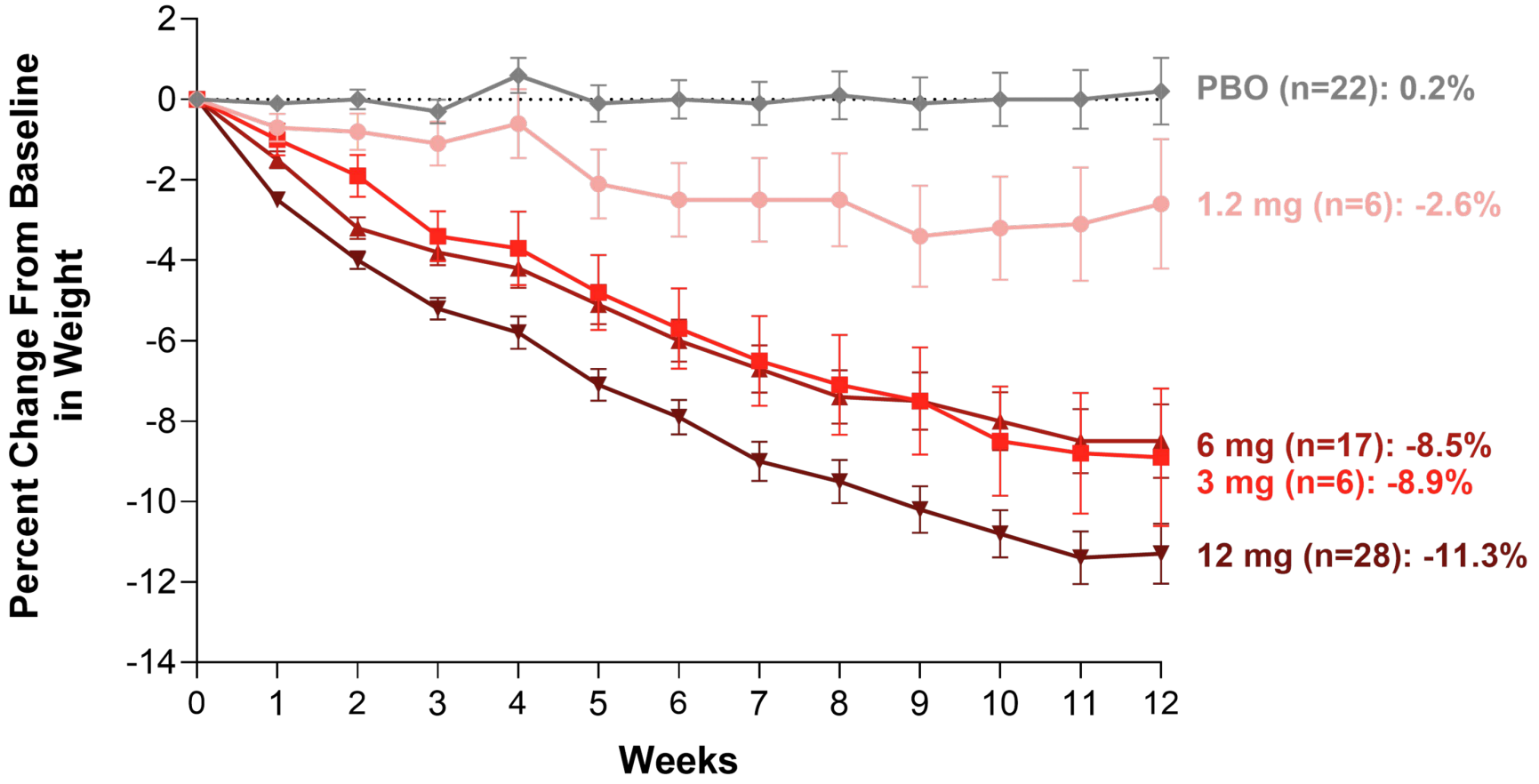


- Eloralintide (LY3841136) is a potent, selective, long-acting amylin receptor agonist that is in development for the treatment of obesity
- Eloralintide exhibits approximately 12-fold greater potency at amylin receptors compared with calcitonin receptors

Phase 1 Study Results: Eloralintide

Achieved Weight Loss at 12 Weeks With No Plateau

- Eloralintide resulted in dose- and time-dependent weight loss in participants with overweight or obesity[1]
- Repeat weekly doses of eloralintide without dose escalation were well tolerated with a low incidence of gastrointestinal AEs

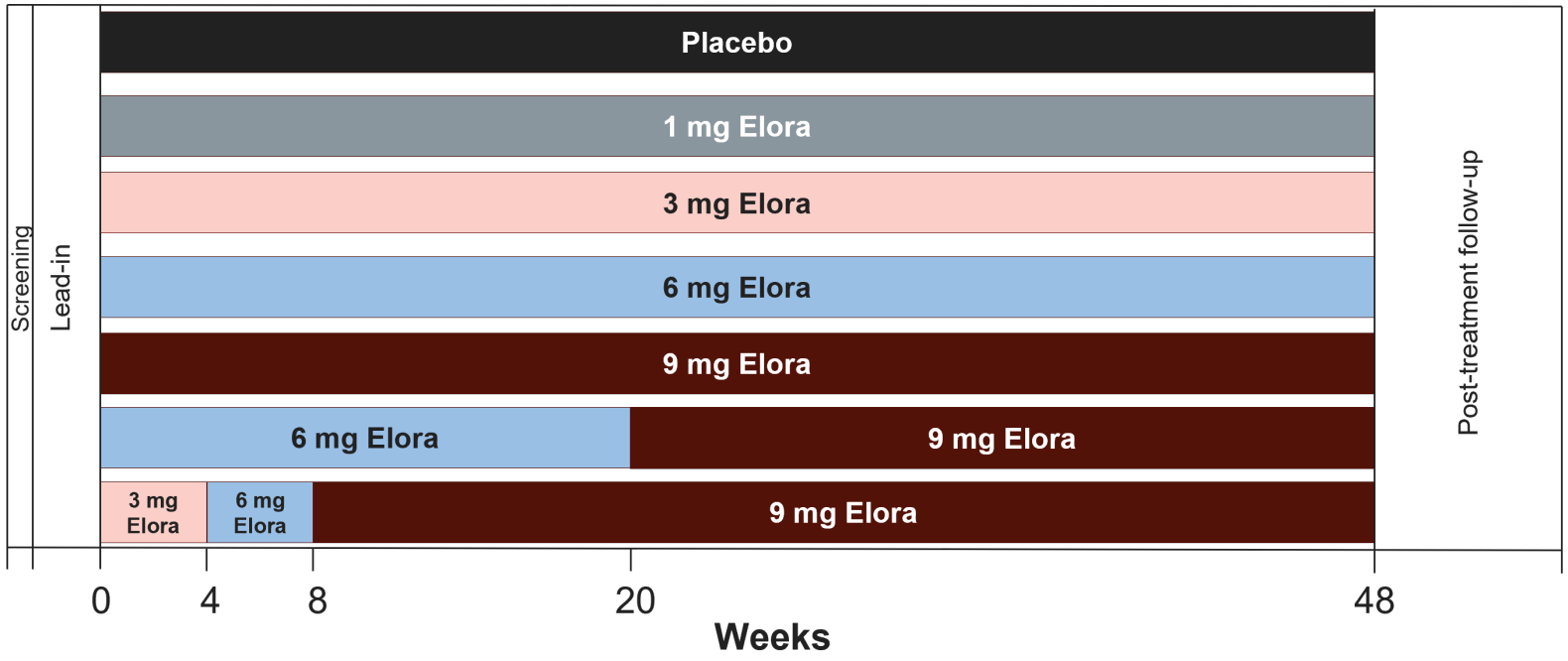


1. Bhattachar SN, et al. *Diabetes*. 2025;74(Suppl 1):882-P.

AE=adverse event; PBO=placebo.

Phase 2 Study Design: Eloralintide

Randomized, Double-Blind, Placebo-Controlled Trial



- Participants were randomly assigned in a ratio of approximately 2:1:1:1:2:1:2 to placebo, 1 mg, 3 mg, 6 mg, 9 mg, 6/9 mg, and 3/6/9 mg eloralintide, respectively
- After completing 48 weeks of treatment, participants were observed over a 10-week follow-up period
- All participants received lifestyle and dietary counseling

Inclusion criteria

- Individuals aged 18 to 75 years
- BMI ≥27 kg/m²
- Stable weight for 3 months prior to randomization (±5% body weight)

Exclusion criteria

- Type 2 diabetes
- Ongoing or history of bradyarrhythmia and/or sinus bradycardia
- History of pancreatitis
- Cardiovascular conditions including acute MI, stroke, unstable angina, or hospitalization due to congestive heart failure
- Treatment with other weight loss medication/surgery

BMI=body mass index; Elora=eloralintide; MI=myocardial infarction.

Primary and Selected Secondary/Exploratory Endpoints

Primary Endpoint

Percent change in weight from baseline at Week 48 compared with placebo

Selected Secondary and Exploratory Endpoints

Secondary

At Week 48,

- Change from baseline in weight (kg)
- Incidence of participants who achieve:
  - ≥5% weight reduction
  - ≥10% weight reduction
- Change from baseline in BMI

Exploratory

At Week 48,

- Change from baseline in:
  - Hb1Ac
  - Fasting glucose
  - Fasting insulin
  - Lipids
  - hs-CRP
- Safety and tolerability

Note: This is not a complete list of secondary and exploratory endpoints for this study.

BMI=body mass index; Hb1Ac=glycated hemoglobin; hs-CRP=high-sensitivity C-reactive protein.

Prespecified Statistical Analyses

Efficacy Analyses

- Conducted on all randomized participants according to the efficacy estimand, where data were included prior to discontinuation of study treatment

Clinical Interpretation of Efficacy Estimand

How will the drug work in clinical practice assuming all are willing and able to take the drug as prescribed?

(Stay ON TREATMENT)

Efficacy estimand was prespecified for Phase 2

Safety Analyses

- Included all randomized participants who received at least 1 dose of eloralintide or placebo, and data were included regardless of study treatment adherence

Baseline Demographics and Clinical Characteristics
Well Balanced Across Groups

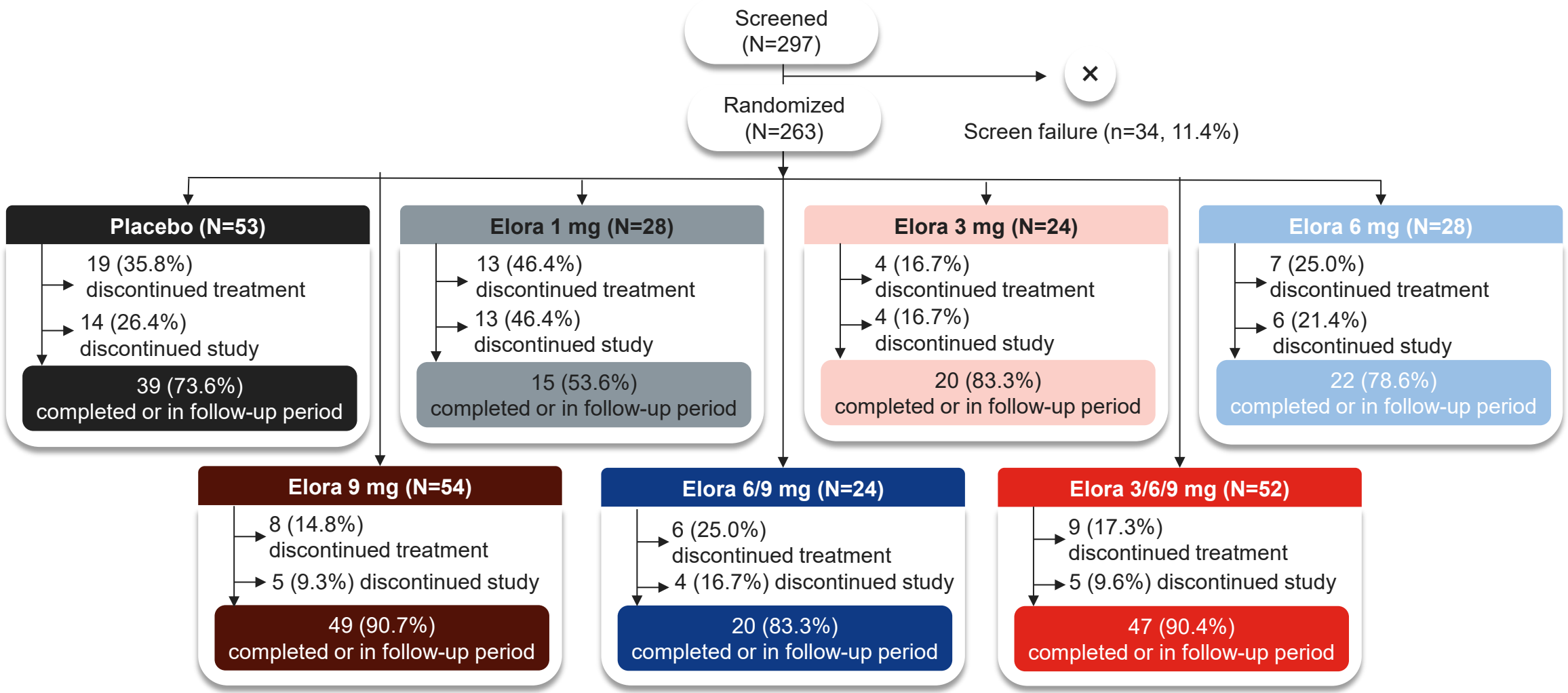
	Placebo	Elora 1 mg	Elora 3 mg	Elora 6 mg	Elora 9 mg	Elora 6/9 mg	Elora 3/6/9 mg	Overall
N (randomized)	53	28	24	28	54	24	52	263
Age, years	48.8 (12.3)	50.4 (13.9)	48.6 (12.2)	46.1 (14.6)	50.2 (12.3)	49.1 (10.9)	48.7 (12.9)	49.0 (12.6)
Female, n (%)	40 (75.5)	21 (75.0)	19 (79.2)	21 (75.0)	43 (79.6)	19 (79.2)	41 (78.8)	204 (77.6)
Race,[a] n (%)								
White	41 (77.4)	21 (75.0)	19 (79.2)	24 (85.7)	39 (72.2)	22 (91.7)	39 (75.0)	205 (77.9)
Black or African American	10 (18.9)	5 (17.9)	4 (16.7)	3 (10.7)	14 (25.9)	2 (8.3)	10 (19.2)	48 (18.3)
Other/Missing	2 (3.8)	2 (7.1)	1 (4.2)	1 (3.6)	1 (1.9)	0	3 (5.8)	10 (3.8)
Weight, kg	109 (22)	113 (35)	108 (19)	107 (18)	107 (17)	110 (25)	111 (24)	109 (23)
BMI, kg/m^2	38.7 (5.7)	40.6 (10.7)	37.9 (5.1)	37.9 (5.9)	38.7 (5.8)	40.3 (7.3)	39.7 (7.1)	39.1 (6.8)
Waist circumference, cm	115 (14)	119 (22)	113 (11)	116 (12)	112 (10)	117 (15)	116 (19)	115 (15)
Glycated hemoglobin level, %	5.5 (0.3)	5.4 (0.4)	5.4 (0.4)	5.4 (0.3)	5.5 (0.4)	5.4 (0.5)	5.5 (0.4)	5.5 (0.4)
Blood pressure, mm Hg								
Systolic	126 (11)	128 (13)	124 (12)	124 (15)	126 (14)	126 (11)	124 (15)	125 (13)
Diastolic	80 (7)	84 (8)	79 (6)	80 (8)	80 (9)	81 (6)	80 (9)	80 (8)

[a]Race and ethnic groups were reported by participants. Other race or ethnic group includes American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific islander, multiple groups, and not reported.

Note: Data are shown as mean (SD) unless stated otherwise.

BMI=body mass index; Elora=eloralintide; SD=standard deviation.

Participant Disposition
Randomization to Week 48



Note: Data are from an interim lock; some participants were still in the study for the safety follow-up at the time of database lock.
Elora=eloralintide.

Phase 2 Monotherapy Study
Design Features and Treatment Disposition

This Phase 2 trial evaluated the weight loss effects of eloralintide, a once-weekly, long-acting, selective amylin receptor agonist

- 263 participants with obesity were randomized to placebo or eloralintide at doses of 1 mg, 3 mg, 6 mg, 9 mg, or dose escalations of 6/9 mg or 3/6/9 mg
- 6 weeks of screening/run-in, followed by 48 weeks of treatment and ~10 weeks of post-treatment follow-up
- Efficacy measures of weight loss, glycemia, and lipids were assessed after 48 weeks, along with safety/tolerability assessments

Eloralintide Phase 2 Study in Adult Participants With Overweight or Obesity: Weight Loss Efficacy

Liana K. Billings, MD, MMSc

Obesity Week 2025; Atlanta, GA; November 4-7, 2025

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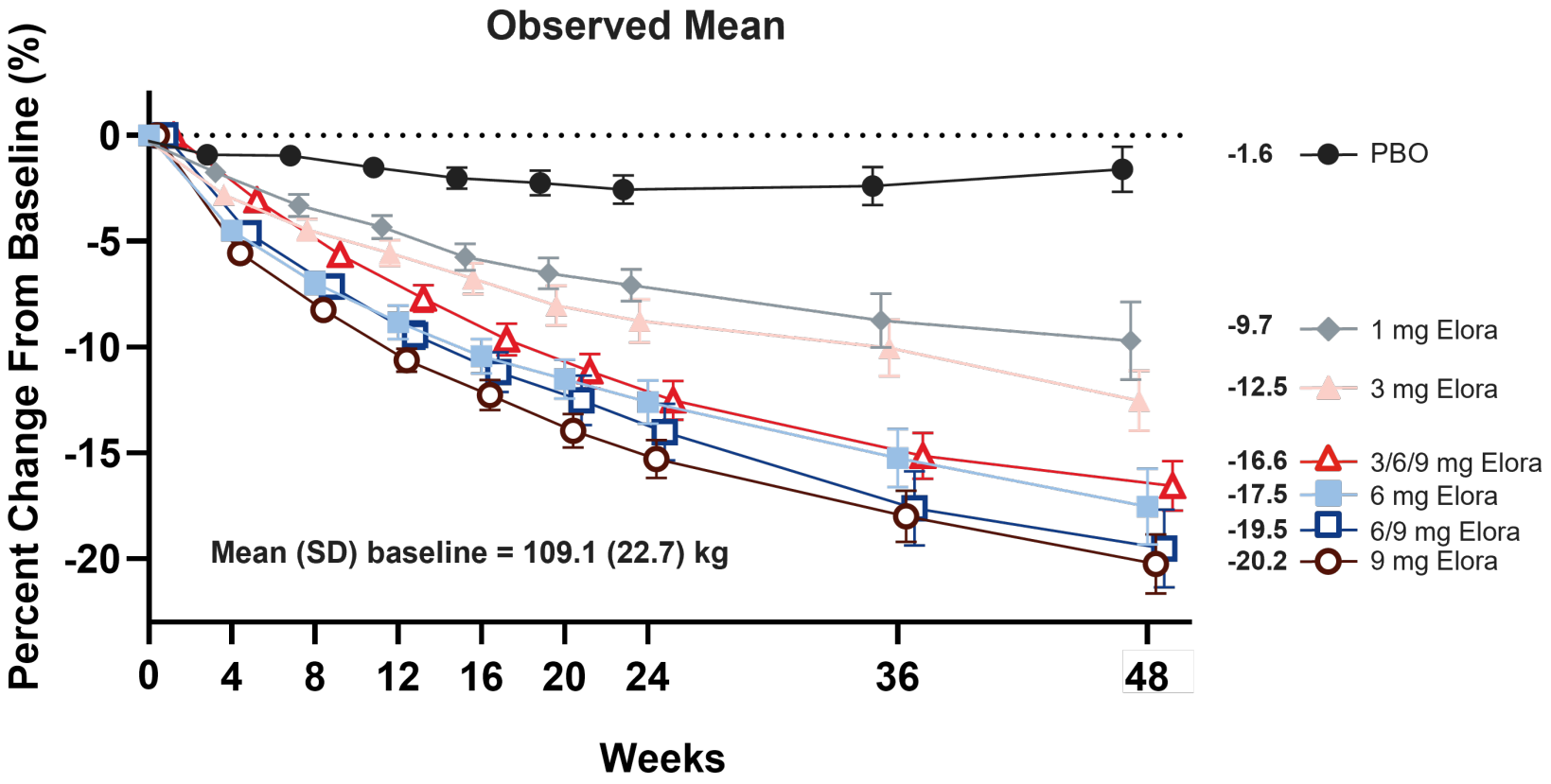
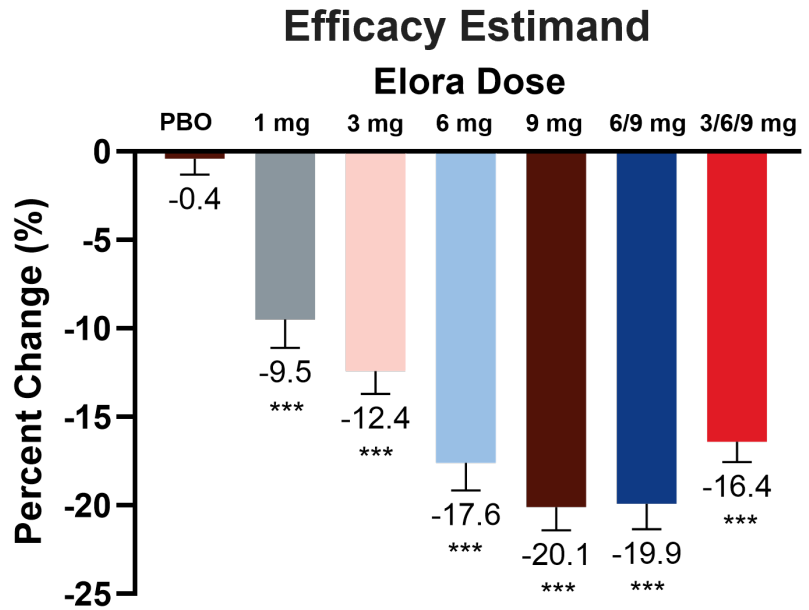
Primary Endpoint:Weight % Change From Baseline

Up to 20% Reduction at 48 Weeks With Eloralintide



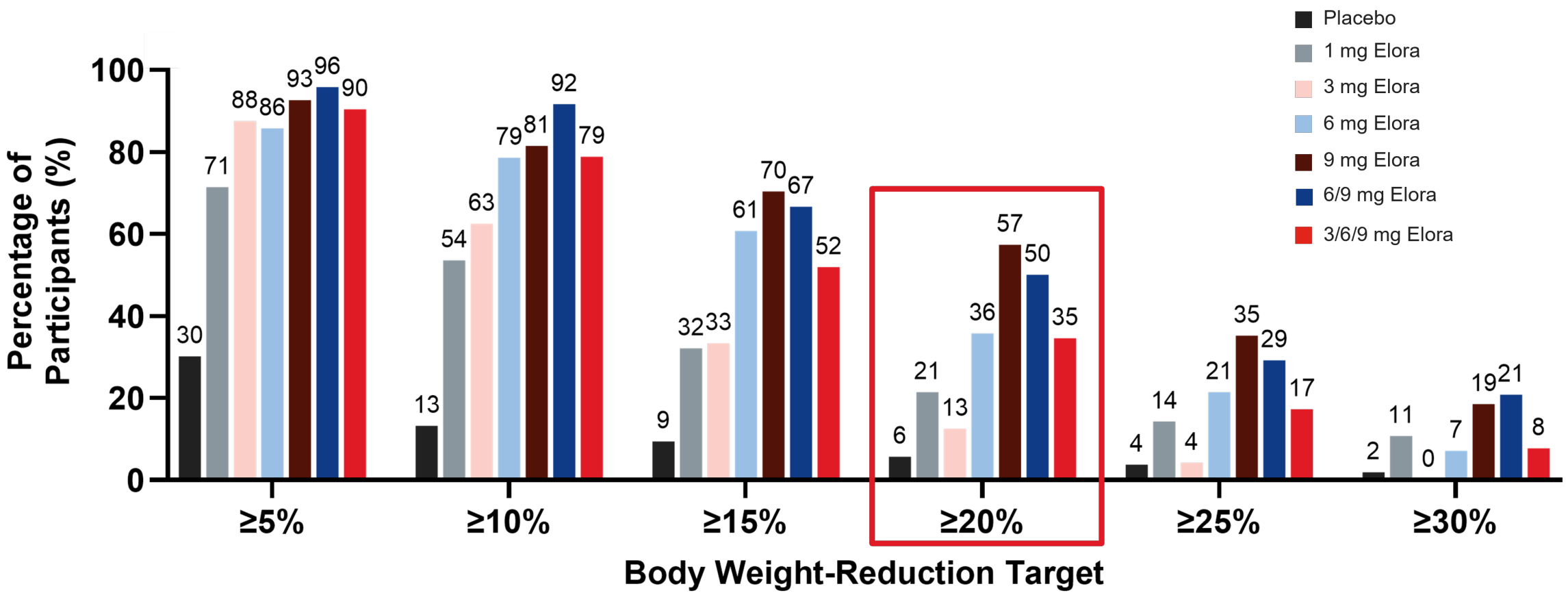


***p<0.001, not adjusted for multiplicity.

Notes: Line graph shows observed mean (SE). Model-based estimates of the means (SE) from an MMRM analysis for the efficacy estimand are shown on the right.

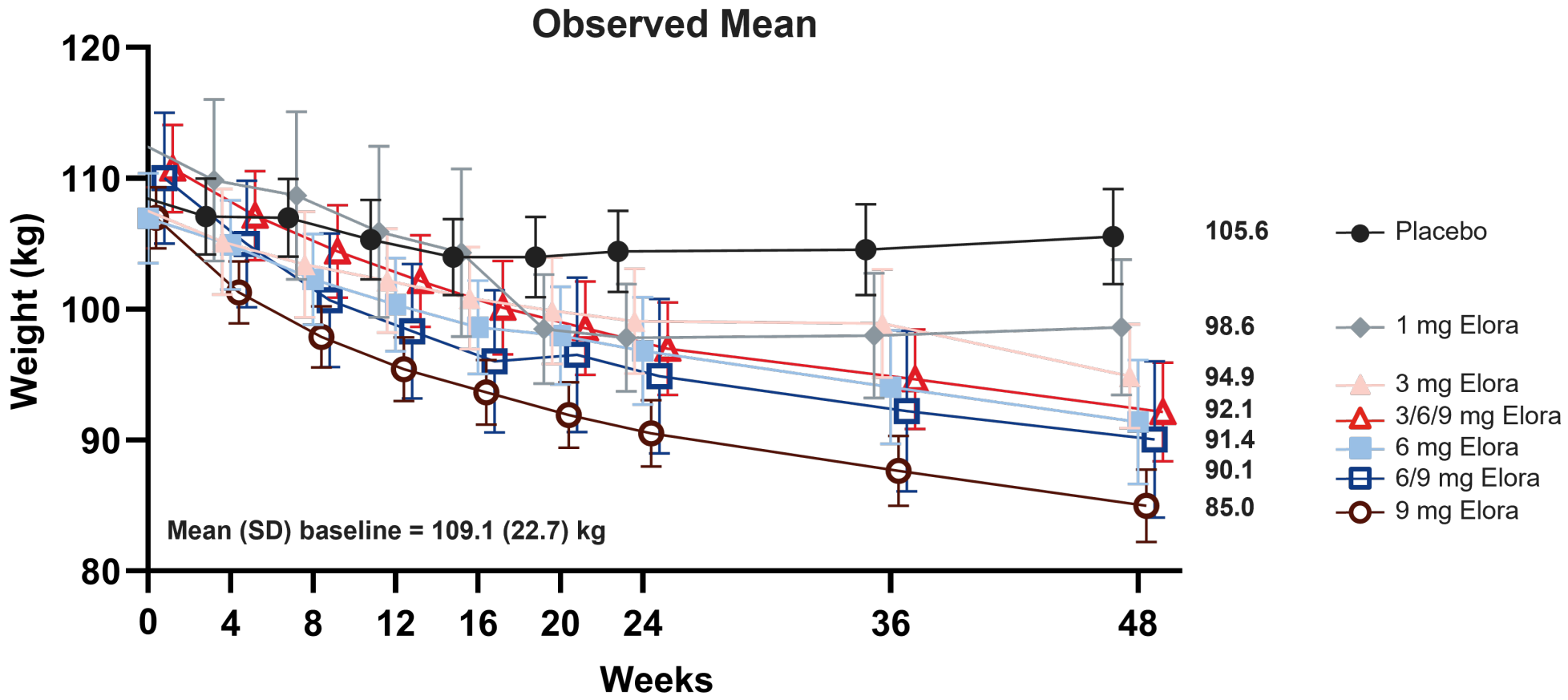
Elora=eloralintide; MMRM=mixed model repeated measures; PBO=placebo; SE=standard error.

Proportion Reaching Weight Reduction Targets:
Up to 57% Treated With Eloralintide Reduced Their Weight by ≥20%



Note: Data calculated with the use of Rubin's rules by combining the percentages of participants who met the thresholds in imputed datasets.
Elora=eloralintide.

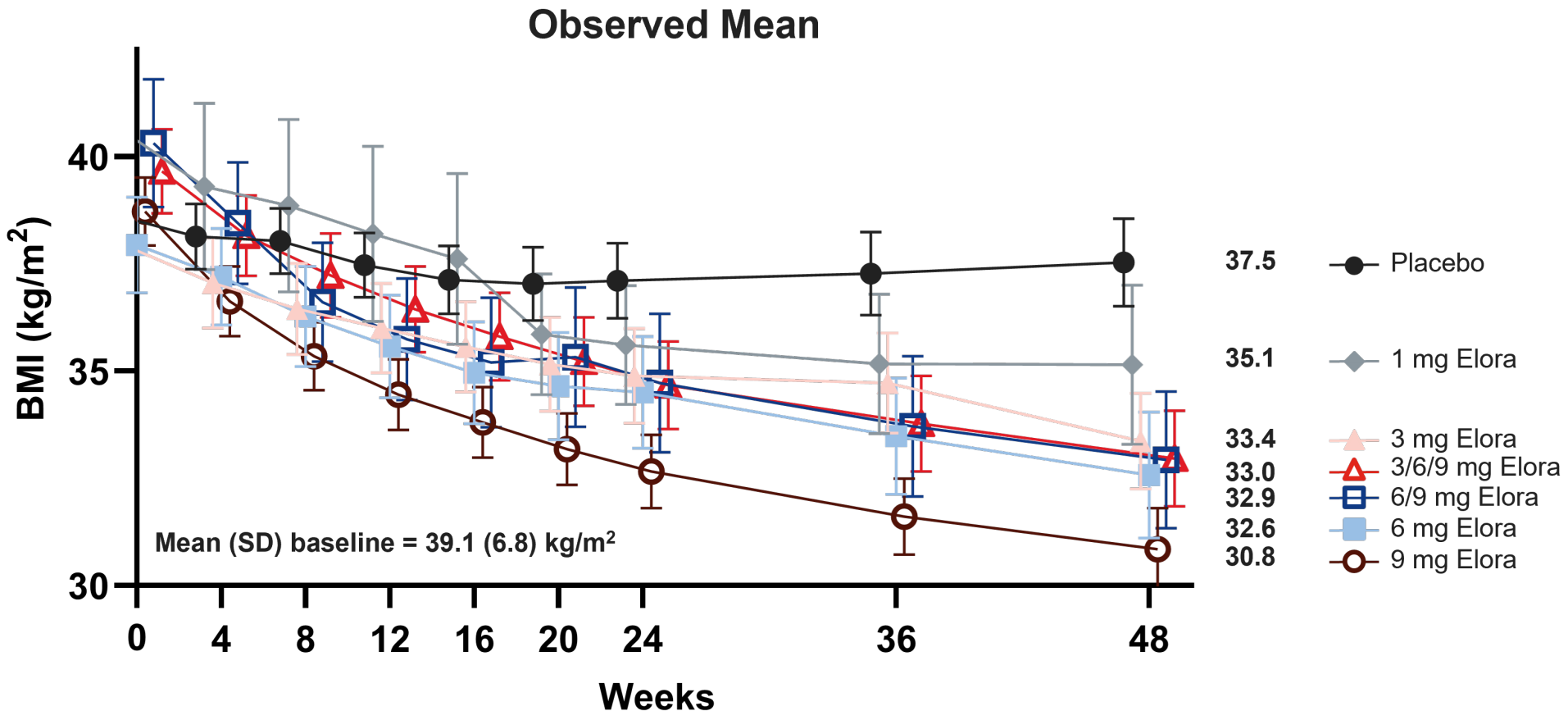
Weight Change From Baseline:
Mean Reduction Up to 21 kg (46 lb) With Eloralintide



Note: Data are shown as observed mean (SE).

Elora=eloralintide; SD=standard deviation; SE=standard error.

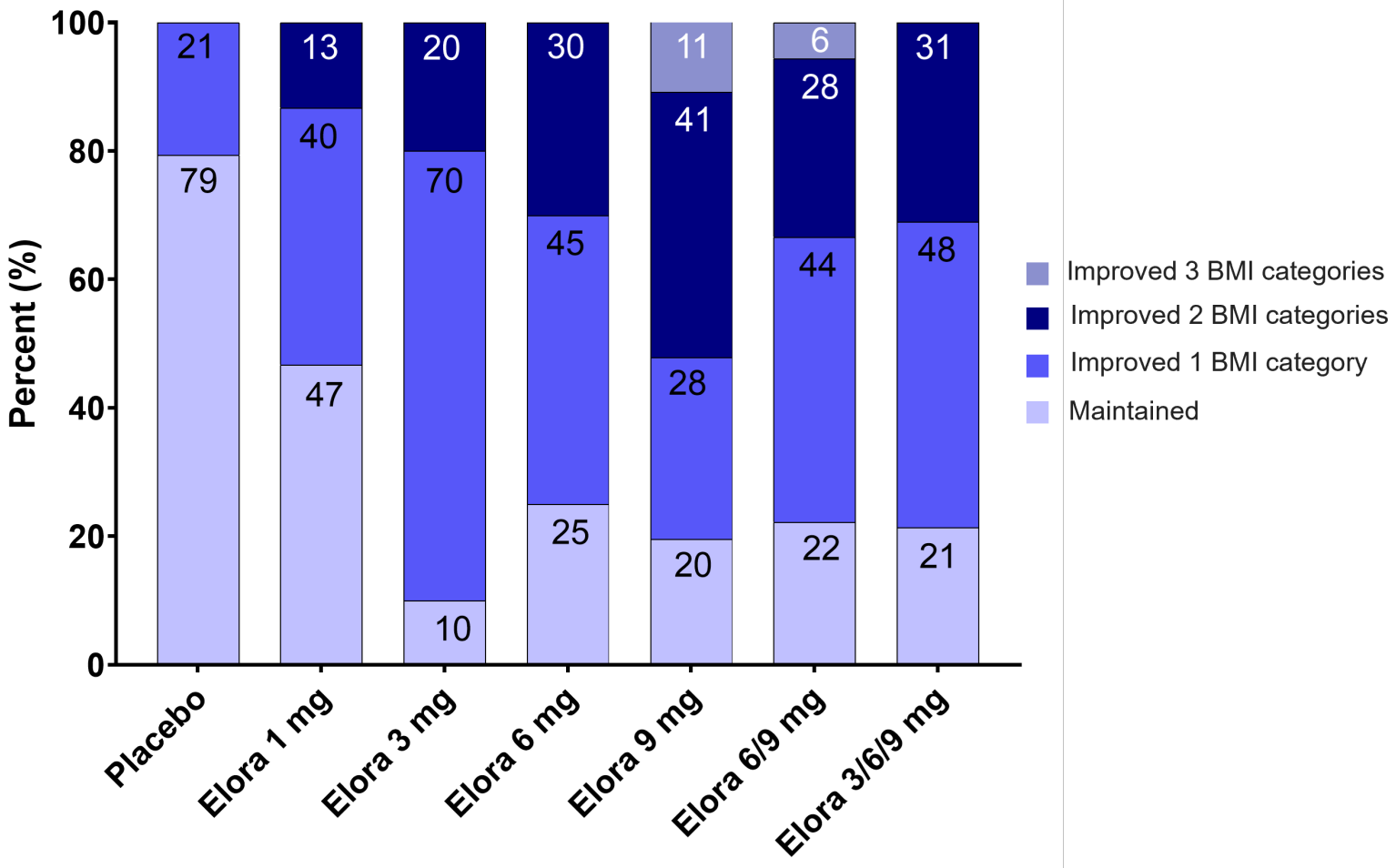
Body Mass Index Change From Baseline:
Reduced Up to 7.9 kg/m^2 With Eloralintide



Note: Data are shown as observed mean (SE).

Elora=eloralintide; SD=standard deviation; SE=standard error.

BMI Category Changes:
Most Participants Improved 1 or More Categories With Eloralintide



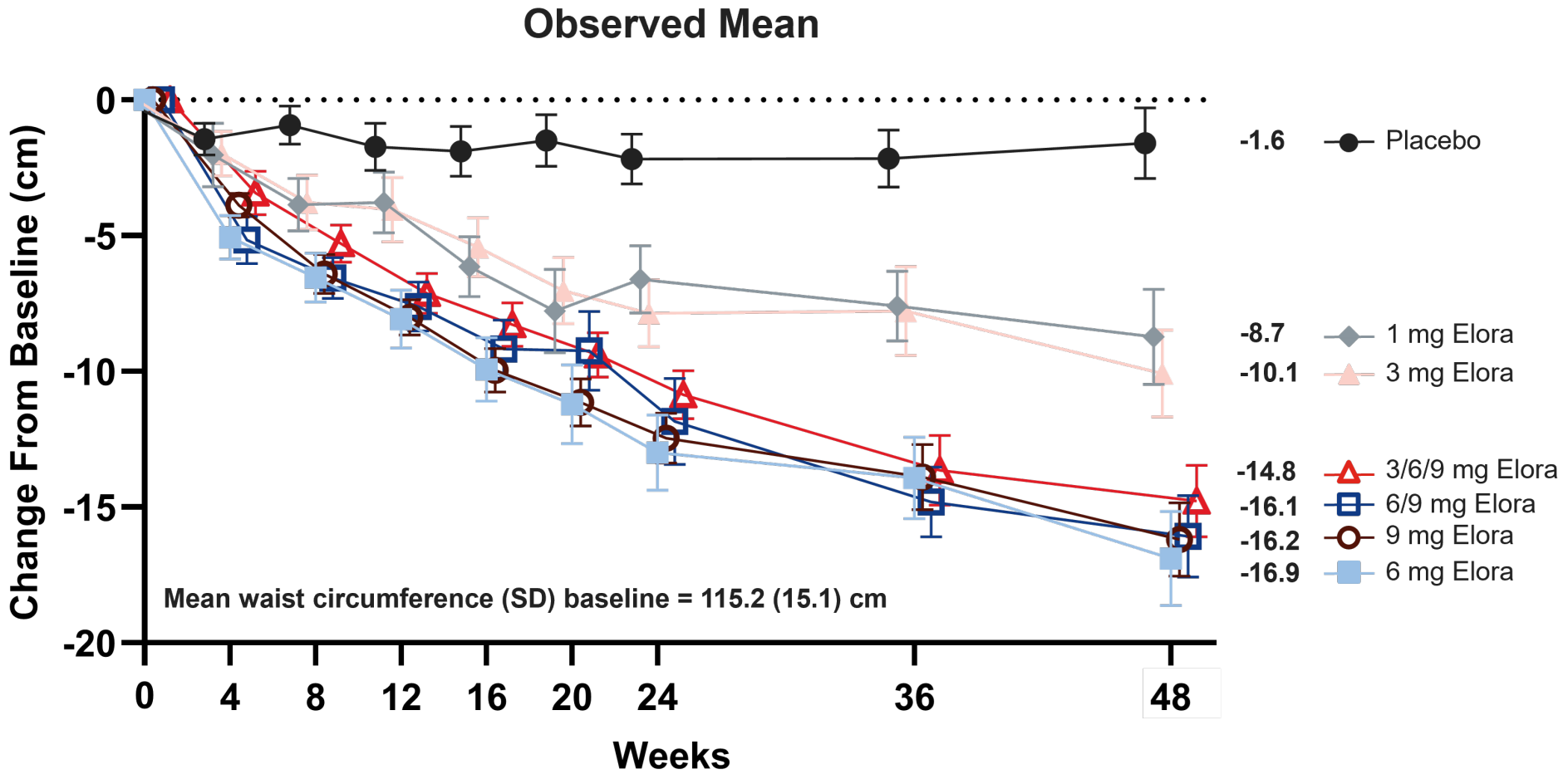
BMI Categories (kg/m²)	
<25	Normal weight
25 to <30	Overweight
30 to <35	Class I Obesity
35 to <40	Class II Obesity
≥40	Class III Obesity

Mean (SD) baseline = 39.1 (6.8) kg/m²

Notes: Measurements were taken between baseline and Week 48. The percentage of participants with BMI recorded at baseline and Week 48 and meeting the respective criteria is given at the top of each bar. No participants worsened in BMI categories.

BMI=body mass index; Elora=eloralintide; SD=standard deviation.

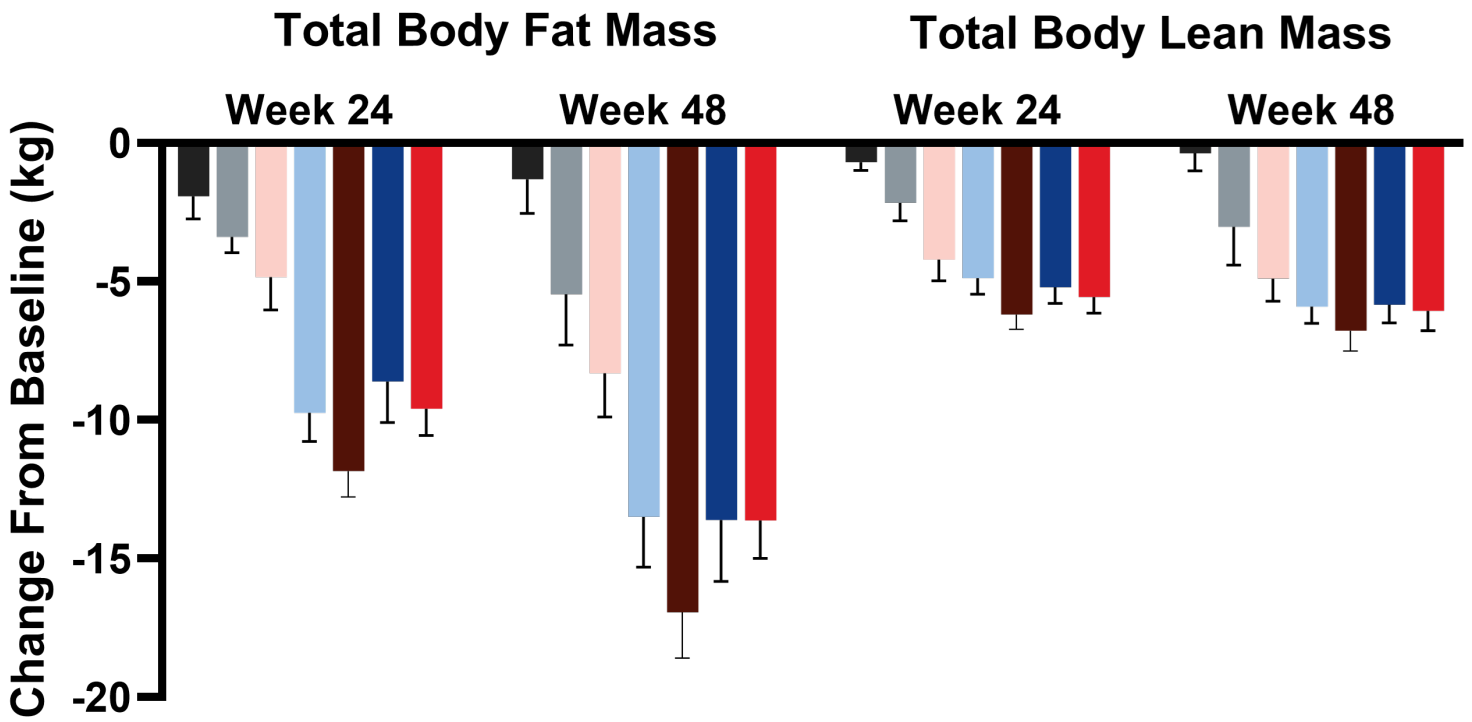
Waist Circumference:
Reduced Up to 16.9 cm (6.7 inches) With Eloralintide



Note: Data are shown as observed mean (SE).

Elora=eloralintide; SD=standard deviation; SE=standard error.

Fat Mass Reduced With Eloralintide in Substudy
60-70% of Mass Reduction Was Due to Fat Loss, on Par With Other Obesity Treatments

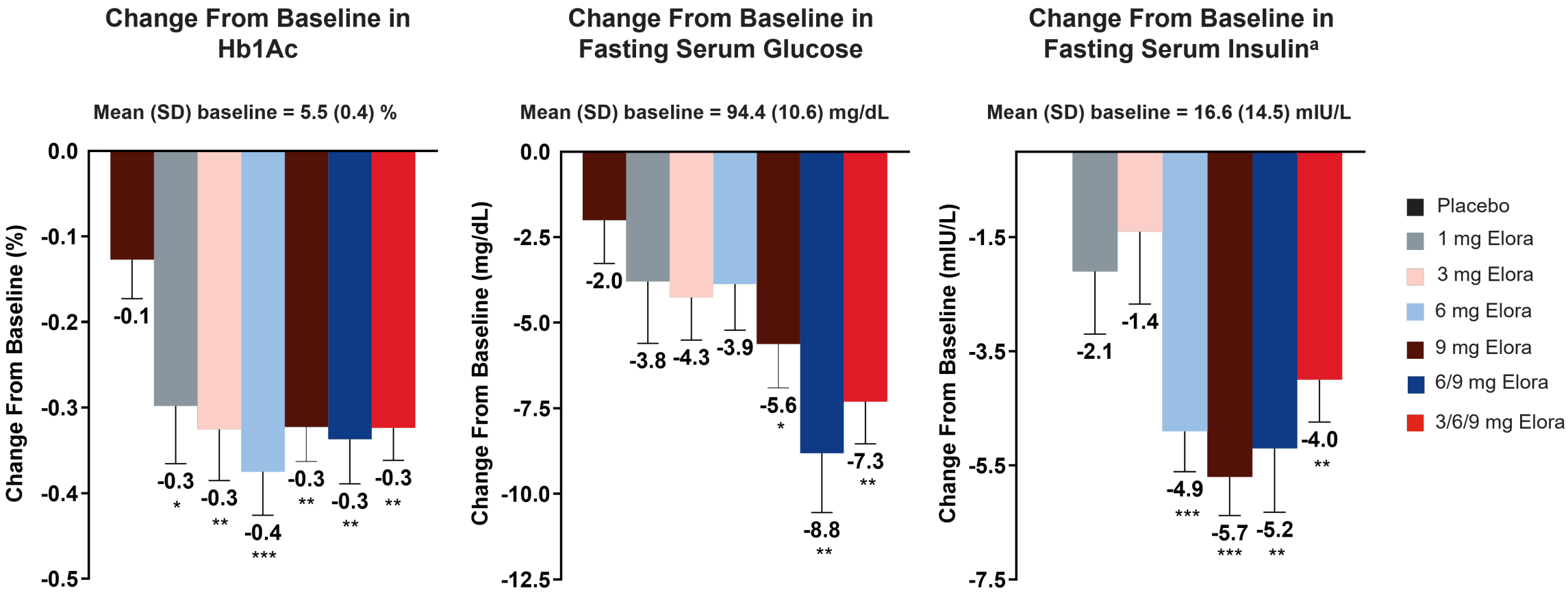


	Fat Loss Index	
	Week 24	Week 48
Placebo	65	46
1 mg Elora	57	62
3 mg Elora	55	64
6 mg Elora	65	71
9 mg Elora	65	72
6/9 mg Elora	60	68
3/6/9 mg Elora	64	69

Notes: Data are from DXA measurements in substudy. Model-based estimates from MMRMs for change from baseline in Lean Mass and change from baseline in Fat Mass were fit separately. The MMRM results were used to calculate the Fat Loss Index, the percentage of mass reduction that is due to fat loss. Week 24: n=135; Week 48: n=122.

DXA=dual X-ray absorptiometry; Elora=eloralintide; MMRM=mixed model repeated measures; SE=standard error.

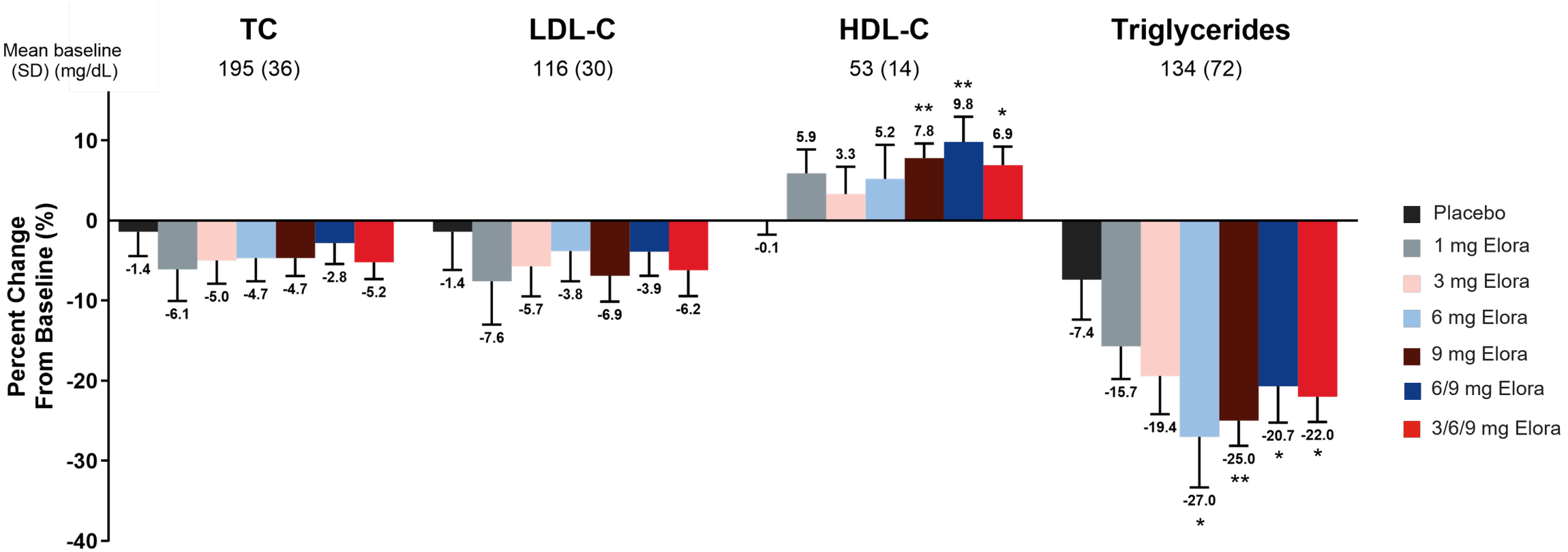
HbA1c and Measures of Fasting Serum Glucose and Fasting Serum Insulin



Elora vs. placebo: *p<0.05, **p<0.01, ***p<0.001; not adjusted for multiplicity. Data shown are model-based estimate (SE). [aDa]ta were log-transformed before fitting the MMRM, then results were back-transformed to the original scale.

Elora=eloralintide; Hb1Ac=glycated hemoglobin; MMRM=mixed model repeated measures; SD=standard deviation; SE=standard error.

Eloralintide Improved Lipid Parameters

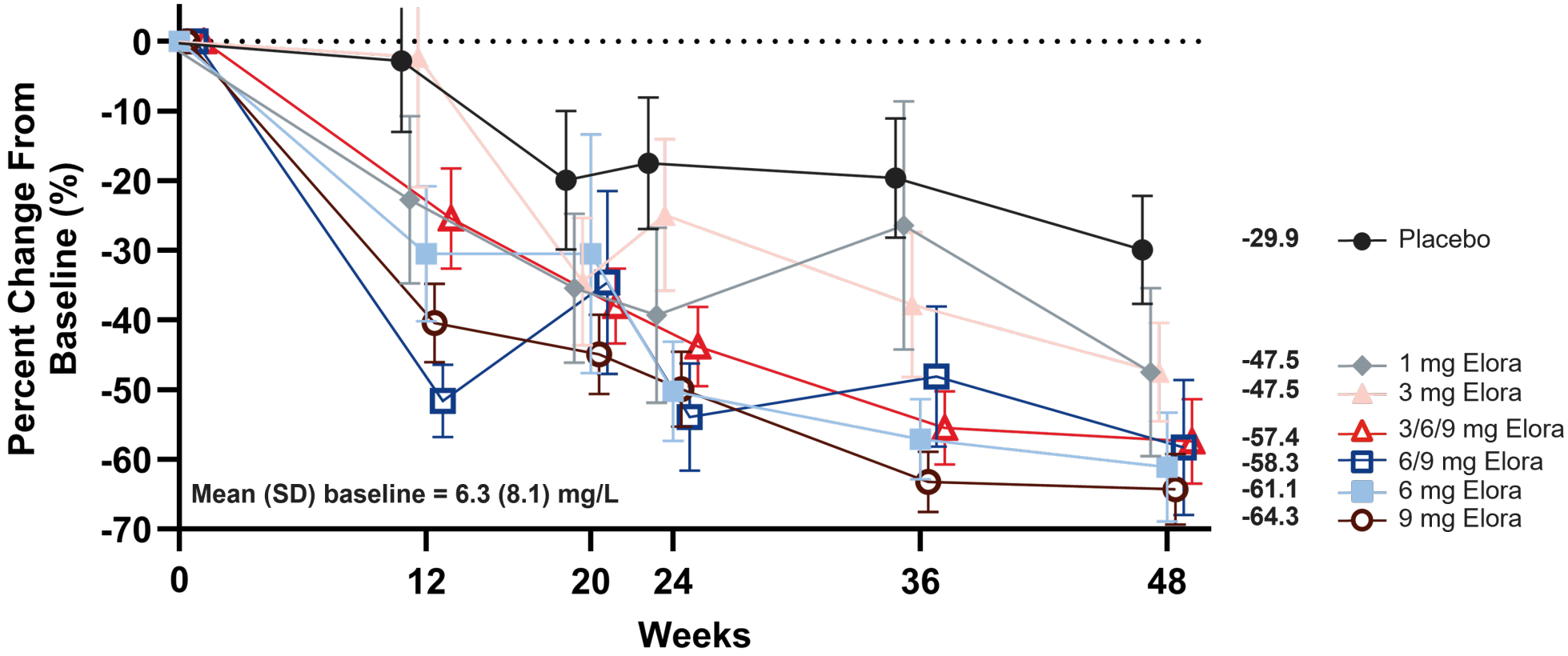


Elora vs. placebo: *p<0.05, **p<0.01. p-values are for estimate difference vs. placebo and were not adjusted for multiplicity.

Notes: Data shown are model-based estimate (SE). Data were log-transformed before fitting the MMRM, then results were back-transformed to the original scale.

Elora=eloralintide; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; MMRM=mixed model for repeated measures; SD=standard deviation; SE=standard error; TC=total cholesterol.

High-Sensitivity C-Reactive Protein
Early and Sustained Reductions With Eloralintide



Notes: Data shown are model-based estimate (SE). Data were log-transformed before fitting the MMRM, then results were back-transformed to the original scale.

Elora=eloralintide; MMRM=mixed model repeated measures; SD=standard deviation; SE=standard error.

Efficacy Summary

- Weight loss was dose responsive with 17%-20% decrease in 9-mg dose maintenance arms
- Up to 90% of eloralintide-treated participants improved by ≥1 BMI category
- With eloralintide, 60%-70% of weight was lost as fat
- HbA1c decreased across all dose arms
- Higher treatment doses improved the lipid profiles
- hsCRP levels fell by over 50% in the higher dose arms

BMI=body mass index; hsCRP=high-sensitivity C-reactive protein.

Eloralintide Phase 2 Study in Adult Participants With Overweight or Obesity: Safety Evaluation

Harold Bays, MD

Obesity Week 2025; Atlanta, GA; November 4-7, 2025

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Summary of Overall Safety Observations

	Placebo	Elora 1 mg	Elora 3 mg	Elora 6 mg	Elora 9 mg	Elora 6/9 mg	Elora 3/6/9 mg	Pooled Elora	Overall
N	**52**	**27**	**23**	**28**	**54**	**24**	**52**	**208**	**260**
All TEAE[a]	37 (71.2)	18 (66.7)	14 (60.9)	28 (100.0)	47 (87.0)	21 (87.5)	41 (78.8)	169 (81.2)	206 (79.2)
AEs leading to discontinuation	4 (7.7)	3 (11.1)	0	6 (21.4)	4 (7.4)	2 (8.3)	6 (11.5)	21 (10.1)	25 (9.6)
Serious AEs	3 (5.8)	3 (11.1)	1 (4.3)	1 (3.6)	3 (5.6)	2 (8.3)	1 (1.9)	11 (5.3)	14 (5.4)
Deaths	0	0	0	0	0	0	0	0	0
TEAEs related to study treatment	25 (48.1)	6 (22.2)	10 (43.5)	25 (89.3)	40 (74.1)	20 (83.3)	33 (63.5)	134 (64.4)	159 (61.2)

[a]Irrespective of causality.

Note: Data are shown as n (%).

AE=adverse event; Elora=eloralintide; TEAE=treatment-emergent AE.

Safety: Most Commonly Observed AEs (≥5%)

GI AEs Common, But Lessened With 4-Week 3/6/9 mg Escalation

	Placebo	Elora 1 mg	Elora 3 mg	Elora 6 mg	Elora 9 mg	Elora 6/9 mg	Elora 3/6/9 mg	Pooled Elora	Overall
N	52	27	23	28	54	24	52	208	260
Nausea	7 (13.5)	3 (11.1)	3 (13.0)	18 (64.3)	18 (33.3)	13 (54.2)	13 (25.0)	68 (32.7)	75 (28.8)
Fatigue	6 (11.5)	0	3 (13.0)	8 (28.6)	23 (42.6)	11 (45.8)	11 (21.2)	56 (26.9)	62 (23.8)
Constipation	3 (5.8)	4 (14.8)	4 (17.4)	2 (7.1)	13 (24.1)	4 (16.7)	4 (7.7)	31 (14.9)	34 (13.1)
Diarrhea	5 (9.6)	1 (3.7)	2 (8.7)	10 (35.7)	6 (11.1)	3 (12.5)	9 (17.3)	31 (14.9)	36 (13.8)
Decreased appetite	2 (3.8)	0	2 (8.7)	4 (14.3)	8 (14.8)	1 (4.2)	5 (9.6)	20 (9.6)	22 (8.5)
Vomiting	0	0	0	7 (25.0)	6 (11.1)	3 (12.5)	1 (1.9)	17 (8.2)	17 (6.5)
COVID-19	2 (3.8)	4 (14.8)	1 (4.3)	3 (10.7)	0	2 (8.3)	4 (7.7)	14 (6.7)	16 (6.2)
Alopecia	0	1 (3.7)	0	1 (3.6)	5 (9.3)	2 (8.3)	5 (9.6)	14 (6.7)	14 (5.4)
Upper respiratory tract infection	6 (11.5)	2 (7.4)	2 (8.7)	2 (7.1)	0	4 (16.7)	3 (5.8)	13 (6.2)	19 (7.3)
Headache	4 (7.7)	0	0	2 (7.1)	3 (5.6)	2 (8.3)	5 (9.6)	12 (5.8)	16 (6.2)

Note: Data are shown as n (%).

AE=adverse event; COVID-19=coronavirus disease 2019; Elora=eloralintide; GI=gastrointestinal.

Adverse Events of Special Interest

	Placebo	Elora 1 mg	Elora 3 mg	Elora 6 mg	Elora 9 mg	Elora 6/9 mg	Elora 3/6/9 mg	Pooled Elora	Overall
N	52	27	23	28	54	24	52	208	260
Hypotension, orthostatic hypotension, and syncope	2 (3.8)	0	2 (8.7)	2 (7.1)	5 (9.3)	1 (4.2)	2 (3.8)	12 (5.8)	14 (5.4)
Acute renal failure	0	0	0	0	0	0	0	0	0
Suicidal ideation and behavior	0	1 (3.7)[a]	0	0	0	0	0	1 (0.5)	1 (0.4)
Depression	1 (1.9)	0	0	1 (3.6)	0	1 (4.2)	1 (1.9)	3 (1.4)	4 (1.5)

[a]The suicidal ideation event was reported 3.5 months after study treatment had been discontinued due to an unrelated adverse event and was deemed by the investigator and the sponsor to be unrelated to study treatment.

Notes: Data are shown as n (%). Adverse events of special interest are prespecified in protocol.

Elora=eloralintide.

Serious Adverse Events

Incidence of SAEs Were Similar Across Treatment Arms

	Placebo	Elora 1 mg	Elora 3 mg	Elora 6 mg	Elora 9 mg	Elora 6/9 mg	Elora 3/6/9 mg	Pooled Elora	Overall
N	52	27	23	28	54	24	52	208	260
Participants with ≥1 SAE	3 (5.8)	3 (11.1)	1 (4.3)	1 (3.6)	3 (5.6)	2 (8.3)	1 (1.9)	11 (5.3)	14 (5.4)
Acute myocardial infarction	0	0	1 (4.3)	0	0	1 (4.2)	0	2 (1.0)	2 (0.8)
Acute kidney injury	0	0	0	0	1 (1.9)	0	0	1 (0.5)	1 (0.4)
Acute respiratory failure	1 (1.9)	0	0	0	0	0	0	0	1 (0.4)
Atrial flutter	0	1 (3.7)	0	0	0	0	0	1 (0.5)	1 (0.4)
Bladder transitional cell carcinoma	1 (1.9)	0	0	0	0	0	0	0	1 (0.4)
Cholelithiasis	0	0	0	0	1 (1.9)	0	0	1 (0.5)	1 (0.4)
Guillain-Barré syndrome	0	0	0	0	1 (1.9)	0	0	1 (0.5)	1 (0.4)
Lymphadenopathy	0	1 (3.7)	0	0	0	0	0	1 (0.5)	1 (0.4)
Mastoiditis	1 (1.9)	0	0	0	0	0	0	0	1 (0.4)
Multiple sclerosis	0	0	0	1 (3.6)	0	0	0	1 (0.5)	1 (0.4)
Musculoskeletal disorder	0	0	0	0	0	1 (4.2)	0	1 (0.5)	1 (0.4)
Small intestinal obstruction	0	0	0	0	0	0	1 (1.9)	1 (0.5)	1 (0.4)
Spontaneous abortion[a]	0	1 (5.0)	0	0	0	0	0	1 (0.6)	1 (0.5)
Suicidal ideation	0	1 (3.7)	0	0	0	0	0	1 (0.5)	1 (0.4)
Thalamic infarction	0	0	0	0	1 (1.9)	0	0	1 (0.5)	1 (0.4)
Transitional cell carcinoma recurrent	1 (1.9)	0	0	0	0	0	0	0	1 (0.4)

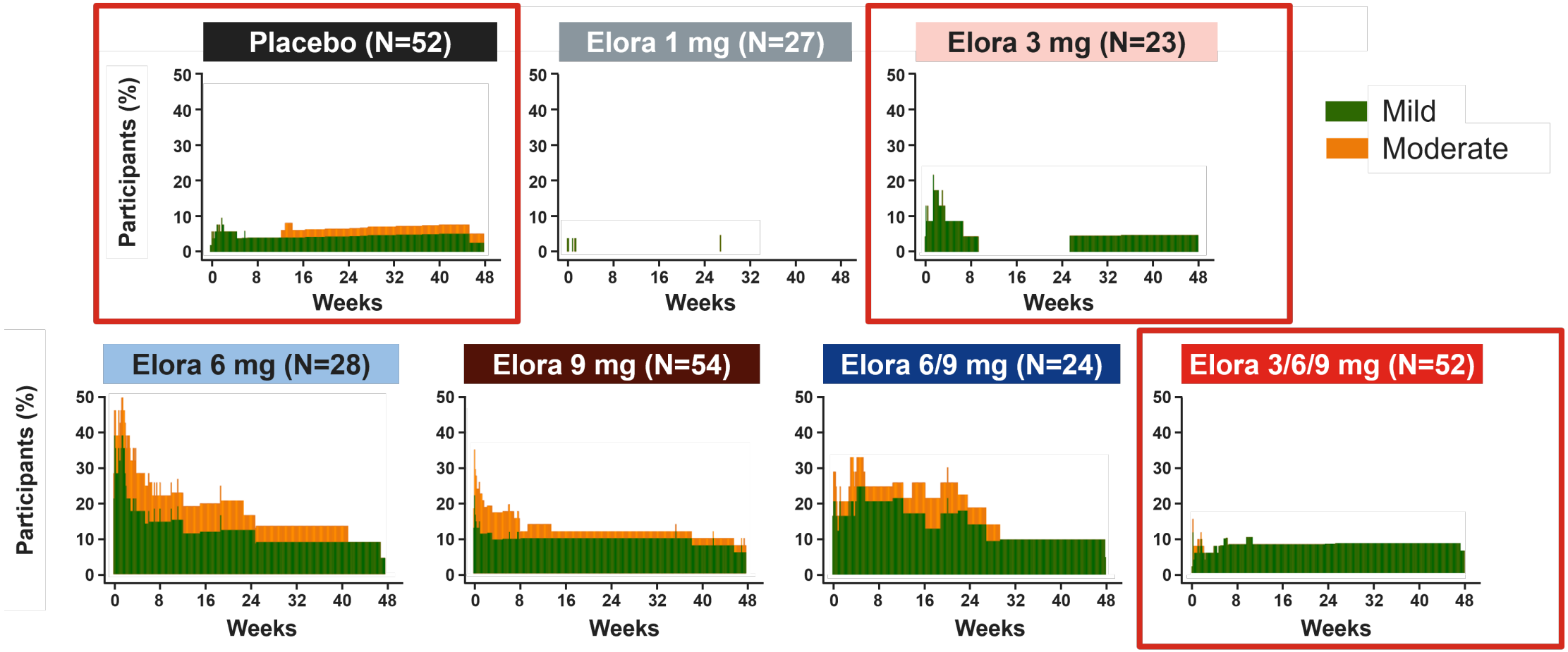
[a]Denominator was adjusted to this being a sex-specific event for females: N=40 (placebo), N=20 (1 mg Elora), N=18 (3 mg), N=21 (6 mg), N=43 (9 mg), N=19 (6/9 mg), N=41 (3/6/9 mg), N=162 (Pooled).
Notes: Data are shown as n (%). SAEs are included if treatment emergent and/or given as the reason for discontinuation of treatment.
Elora=eloralintide; SAE=serious adverse event.

GI Adverse Events and Fatigue Were Generally Mild to Moderate in Severity

	Placebo	Elora 1 mg	Elora 3 mg	Elora 6 mg	Elora 9 mg	Elora 6/9 mg	Elora 3/6/9 mg	Pooled Elora	Overall
N	52	27	23	28	54	24	52	208	260
Gastrointestinal events									
Mild	17 (32.7)	9 (33.3)	8 (34.8)	17 (60.7)	18 (33.3)	9 (37.5)	23 (44.2)	84 (40.4)	101 (38.8)
Moderate	3 (5.8)	0	1 (4.3)	6 (21.4)	13 (24.1)	7 (29.2)	4 (7.7)	31 (14.9)	34 (13.1)
Severe[a]	0	1 (3.7)	0	0	2 (3.7)	0	1 (1.9)	4 (1.9)	4 (1.5)
Fatigue									
Mild	6 (11.5)	0	2 (8.7)	4 (14.3)	16 (29.6)	9 (37.5)	9 (17.3)	40 (19.2)	46 (17.7)
Moderate	0	0	1 (4.3)	4 (14.3)	7 (13.0)	2 (8.3)	2 (3.8)	16 (7.7)	16 (6.2)
Severe	0	0	0	0	0	0	0	0	0

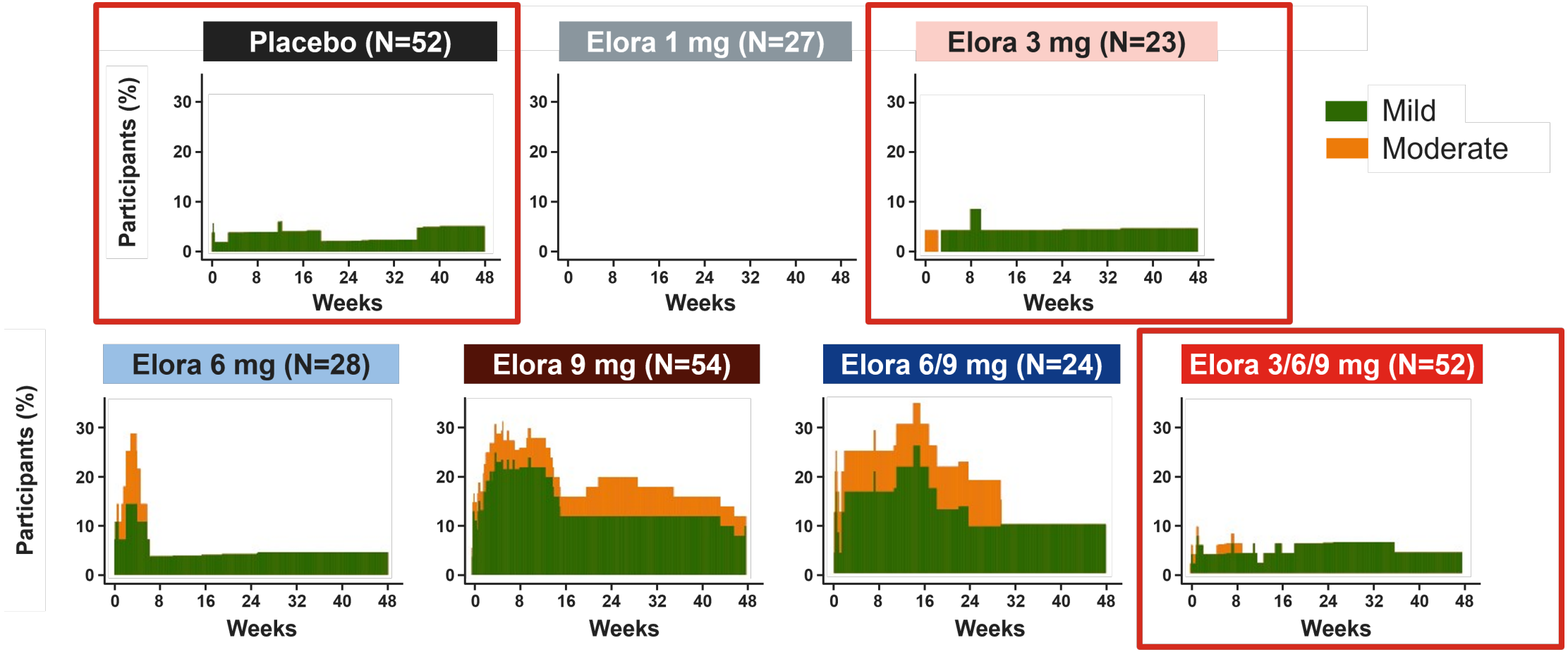
[a]There were 4 cases of severe constipation.
Note: Data are shown as n (%).
Elora=eloralintide.

Prevalence of Nausea, Diarrhea, and Vomiting (Combined): Moderated With 3/6/9 mg Escalation



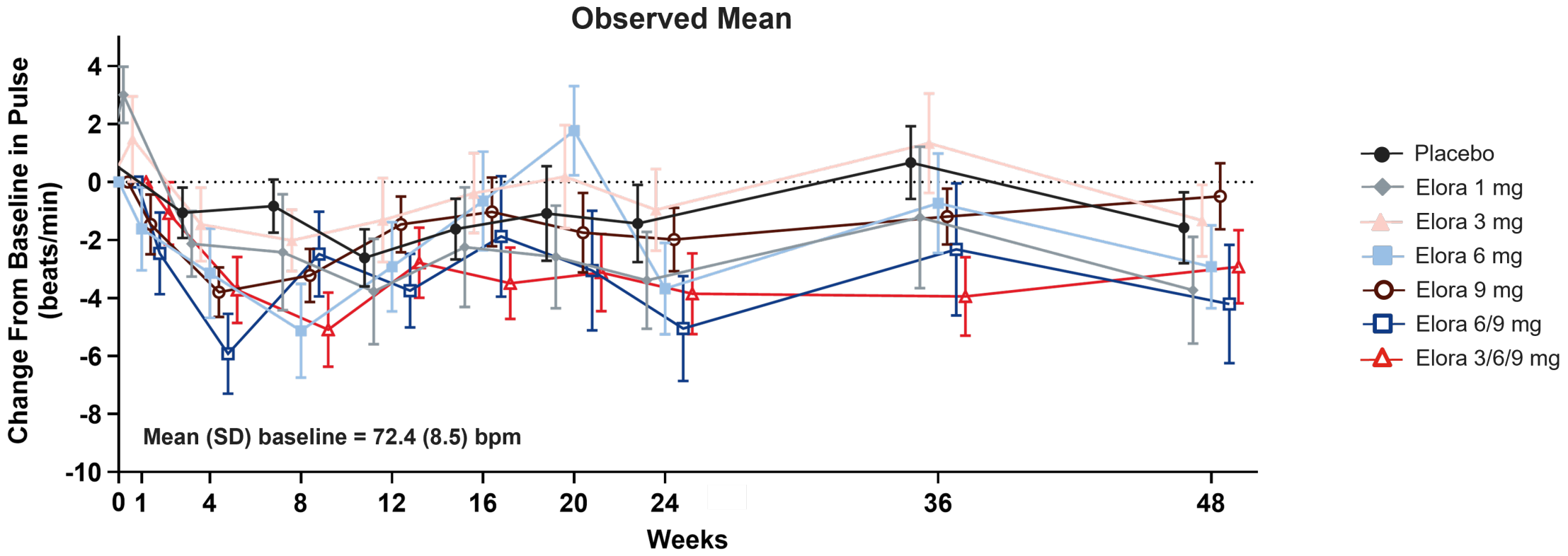
Note: There were no incidents of severe nausea, diarrhea, or vomiting.
Elora=eloralintide.

Prevalence of Fatigue: Moderated With 3/6/9 mg Escalation



Notes: Fatigue is based on the preferred term of "Fatigue." There were no incidents of severe fatigue.
Elora=eloralintide.

Pulse Rate
Early and Sustained Reductions

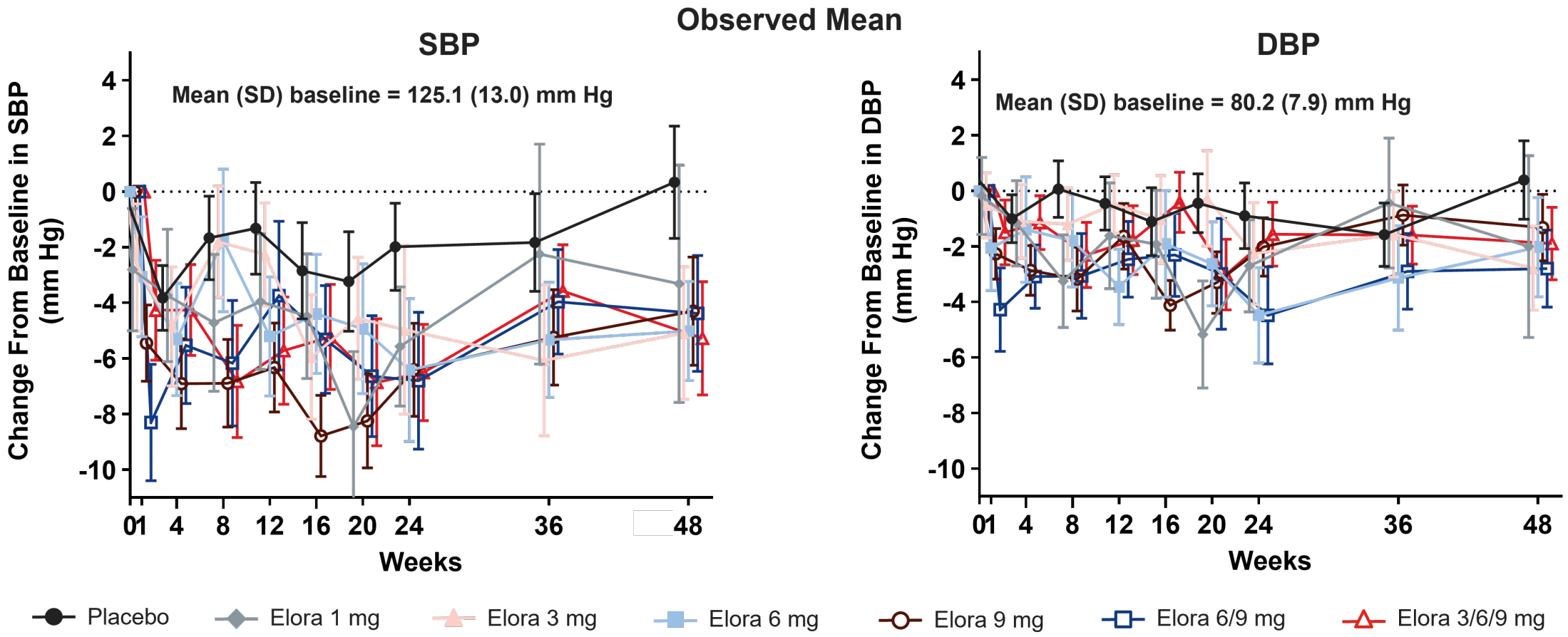


- 13 (6.3%) eloralintide participants were reported to have bradycardia adverse events

Note: Data are shown as observed mean (SE). Reports of bradycardia were investigator reports and not based upon handling plans with defined cut-off points.

bpm=beats per minute; Elora=eloralintide; SD=standard deviation; SE=standard error.

Blood Pressure
Early and Sustained Reductions



Note: Data are shown as observed mean (SE).

DBP=diastolic blood pressure; Elora=eloralintide; SBP=systolic blood pressure; SD=standard deviation; SE=standard error.

Safety Summary

- Reports of GI AEs and fatigue that appear to be dose related
- AEs appeared to be reduced with dose escalation (3/6/9 mg)
- Adverse experiences were typically mild to moderate with reduced frequency over time
- Pulse rate and systolic and diastolic blood pressures were reduced in arms treated with eloralintide
- Safety labs overall revealed no clinically meaningful observations

AE=adverse event; GI=gastrointestinal.

Overall Conclusions
Phase 2 Eloralintide

- Eloralintide, a selective amylin receptor agonist, is being developed as a potential therapeutic option for obesity
- Eloralintide produced clinically meaningful, dose-dependent reductions in weight over 48 weeks among adults with overweight or obesity with an acceptable tolerability profile, particularly when dose escalation was used
- Eloralintide may expand weight loss treatment options for patients unable to achieve adequate benefit from or tolerate existing obesity treatments
- These findings support eloralintide as a potential addition to the expanding therapeutic landscape for obesity, alone or in combination with incretins