CBeyond

Phase 2a Topline Clinical Data

October 2025

Nasdaq: SKYE

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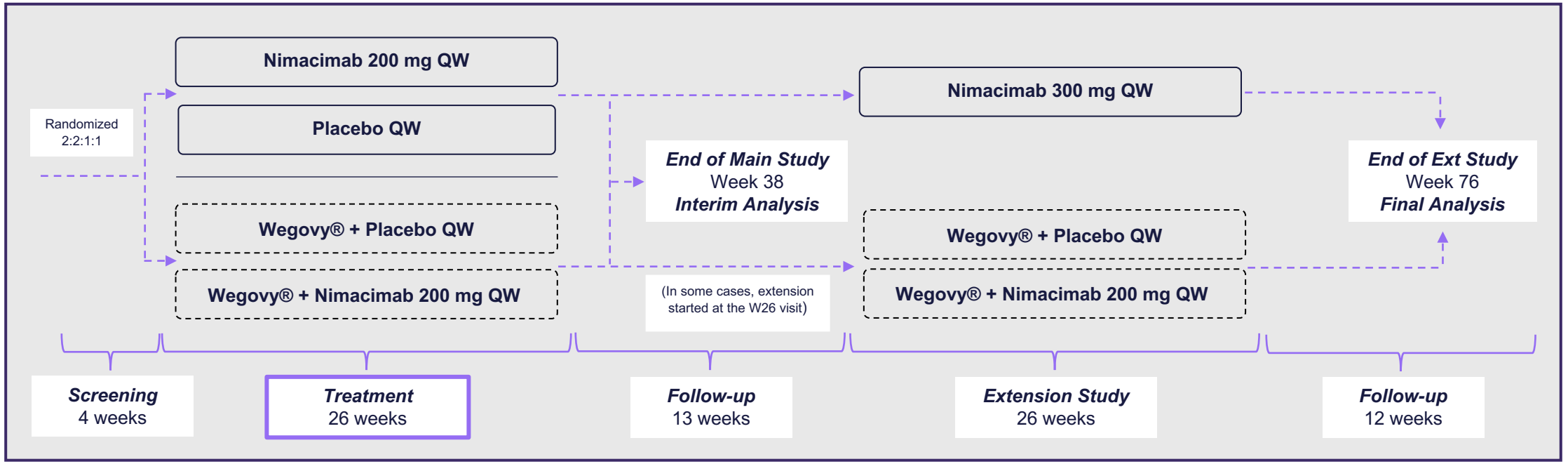
Agenda

1. Introduction
2. Phase 2a Topline Data Overview
3. Safety and Tolerability
4. Summary and Path Forward
5. Questions & Answer Session

CBeyond Phase 2a Trial Data Overview

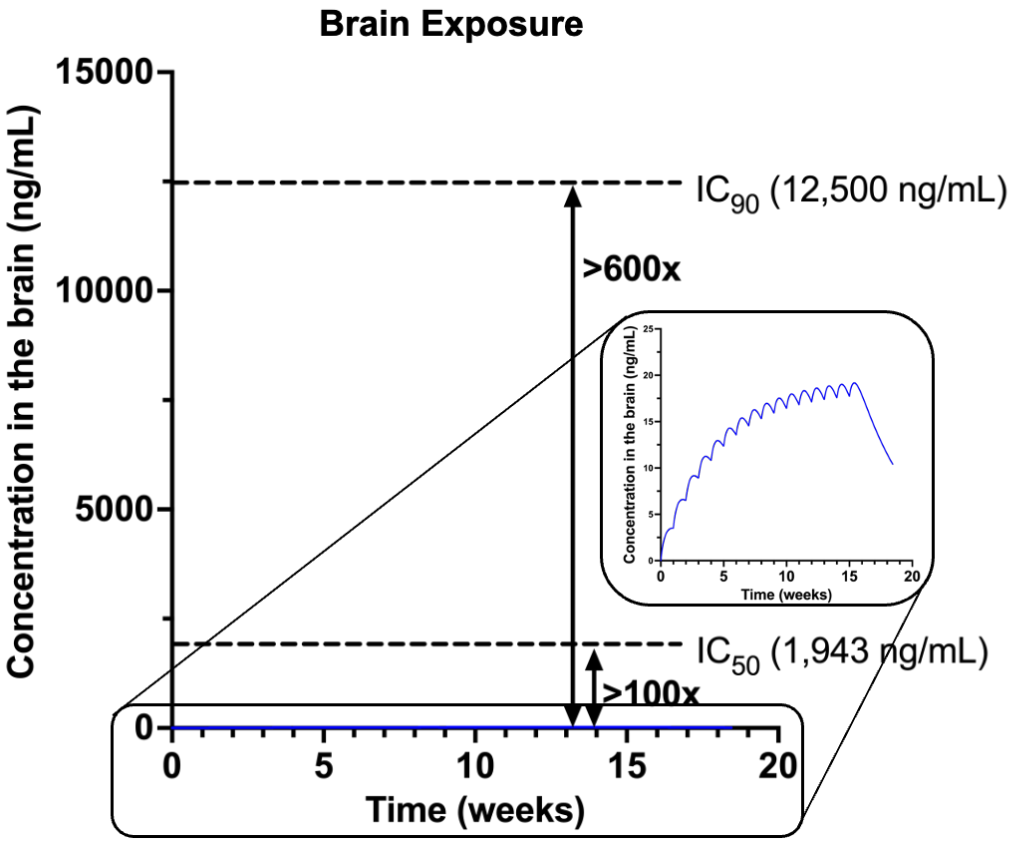
CBeyond Phase 2a Study Design

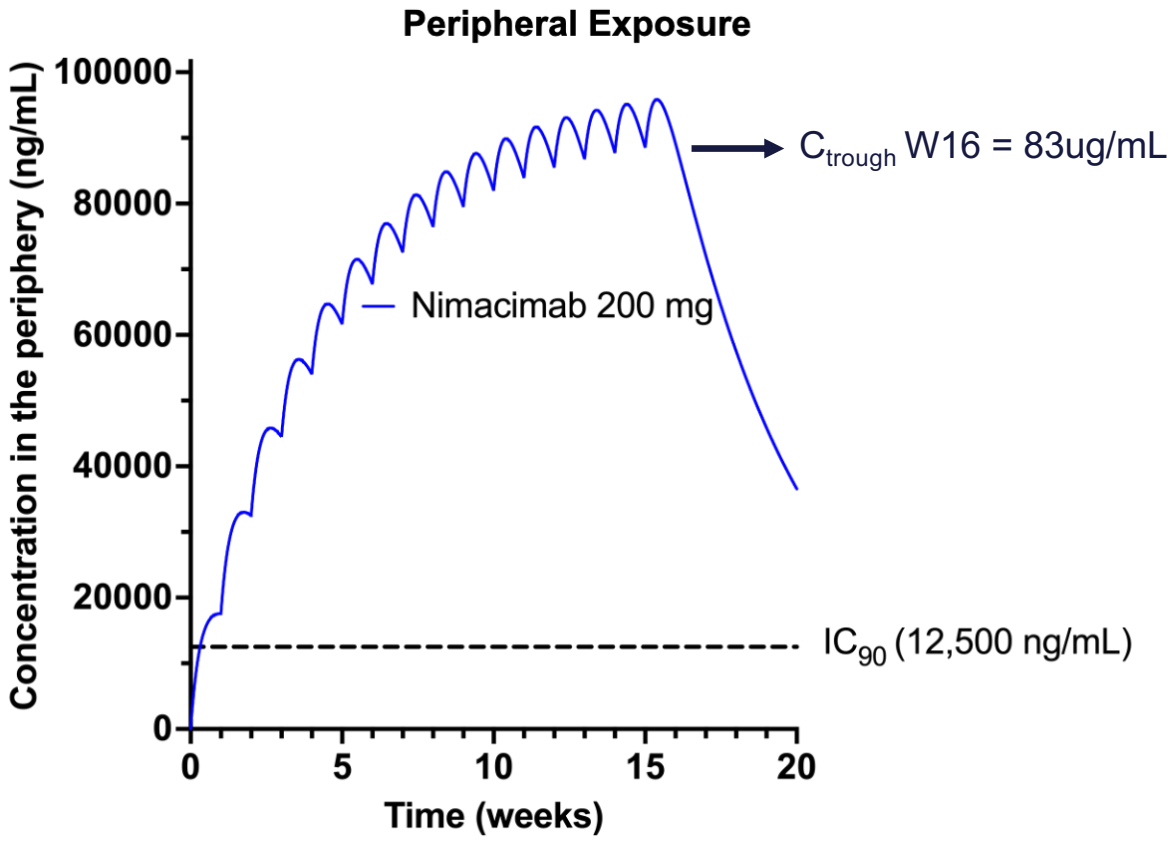
Patients with Overweight or Obesity



Initial 26-week treatment period completed, and 26-week extension study is ongoing

PK Model / Rationale for 200 mg Dosing





- 200 mg QW dose for CBeyond was selected based on modeling from nimacimab Phase 1 studies.
- These models suggested significant peripheral exposure over 26 weeks with little to no exposure in the brain.
- We believed this dosing would demonstrate weight loss without neuropsychiatric concerns.

Datasets for Analysis

mITT (modified Intention to Treat)

- All participants who were randomized and who received any amount of study medication (IP, active or placebo comparator), regardless of adherence to the treatment plan. For analyses, participants were included in the treatment group corresponding to the study treatment they actually received.

- 7 patients initially randomized to monotherapy were treated as combination patients and received semaglutide at all time points. These patients were included in the treatment group that corresponded to the study treatment they received.

PP (Per Protocol)

- All participants in the mITT who adhered to the protocol and did not have any major protocol deviations that could have an impact on the primary study outcomes.

Primary Estimand for Analysis

Intercurrent events resulting in missing data were handled using a treatment policy strategy.

All data collected was included in the analysis and observations were used without adjustment.

The following are the possible intercurrent events:

- Lost to follow-up prior to Week 26
- Initiation of off-study anti-obesity medication
- Initiation of bariatric surgery or other weight-reducing procedures
- Treatment discontinuation prior to Week 26
- Death before Week 26

Population level summaries are presented as the difference in least-squares mean percent change in body weight at Week 26 between treatment groups as estimated from the Mixed Model for Repeated Measures (MMRM) under the assumption of data being Missing At Random.

No explicit imputation for the missing observations was performed.

CBeyond Phase 2a Topline Data Outcome

	Endpoint *(Topline Read)*	Expectations to support TPP	26-Week Results
❌ 1	**Efficacy: % Weight Loss Mono** *Absolute and placebo-adjusted weight loss at 26 weeks*	5-8% (placebo-adjusted)	**Primary endpoint not met**: Nimacimab monotherapy did not achieve the primary endpoint of weight loss compared to placebo (-1.26%, p=0.2699, mITT and -1.33%, p=0.2878, PP) **Potential relationship to exposure**: Preliminary association between exposure and weight loss with nimacimab was observed. The majority of patients did not have the expected exposure to nimacimab.
✅ 2	**Combo Efficacy: % Weight Loss** (GLP-1 Combination) *Absolute and placebo-adjusted weight loss at 26 weeks* *Directional additivity vs GLP-1 alone*	CB1 + GLP-1: PoC (Look for additivity signals)	**Combo** showed a clinically meaningful placebo-subtracted weight loss compared to semaglutide alone (-12.9% vs -9.99%, p=0.0372, mITT and -14.3% vs -10.8%, p=0.0178, PP). Supports path to **increased WL** with no worsening of **tolerability**.
✅ 3	**GI Tolerability** (Mono & Combo) *Nausea/vomiting/diarrhea; discontinuations related to GI*	Lower GI Burden	**Observed low GI burden**: no difference in GI AEs for nimacimab monotherapy vs placebo and no additive GI AEs for nimacimab + GLP-1 combo vs GLP-1 alone.
✅ 4	**Safety** (incl. neuropsychiatric) *26-week summary; Looking for any neuropsychiatric signals and other safety concerns*	No Neuropsychiatric	**Very clean safety. No neuropsychiatric adverse events.**
✅ 5	**Body Composition** *Fat vs. lean mass (DEXA)*	Preferential fat loss	**Improved lean mass to fat mass ratio** was observed in the combination arm at Week 26 compared to the semaglutide-alone arm (0.26 vs. 0.13, p = 0.0126).
⏱ 6	**Metabolic Biomarkers** *(exploratory)* *Directionality in insulin resistance, lipids, ALT, adiponectin*	Support peripheral CB1 biology	**Data not yet available.**

Subject Disposition & Demographics

	Nimacimab 200 mg	Placebo	Nimacimab 200 mg + Semaglutide	Placebo + Semaglutide	Overall
Participants Randomized	45	46	23	22	136
Primary Study Period Withdrawal	13 (28.9%)	14 (30.4%)	6 (26.1%)	4 (18.2%)	37 (27.2%)
Mean Subject Age (SD)	45.5 (12.74)	44.6 (12.70)	44.7 (14.06)	49.0 (12.47)	45.6 (12.92)
Male / Female	17.5% / 82.5%	11.4% / 88.6%	21.4% / 78.6%	12.5% / 87.5%	15.4% / 84.6%
Mean Baseline Weight (SD)	107.31 (21.29)	101.17 (16.41)	101.29 (18.87)	92.28 (14.18)	102.14 (18.35)
Mean Baseline BMI (SD)	37.27 (5.29)	36.86 (4.81)	37.05 (4.67)	35.86 (4.30)	36.84 (4.82)

SD = Standard Deviation; All weights are in kg

Primary Reason for Withdrawal from Primary Study Period

	Nimacimab 200 mg	Placebo	Nimacimab 200 mg + Semaglutide	Placebo + Semaglutide	Overall
Participants Randomized	45	46	23	22	136
Lost to Follow-up	3 (6.7%)	2 (4.3%)	1 (4.3%)	1 (4.5%)	7 (5.1%)
Protocol Deviation	1 (2.2%)	0	1 (4.4%)	0	2 (1.5%)
Adverse Event	1 (2.2%)	3 (6.5%)	1 (4.4%)	0	5 (3.7%)
Study Terminated by Sponsor	0	0	0	0	0
Physician Decision	0	0	0	0	0
Withdrawal by Subject	7 (15.6%)	9 (19.6%)	2 (8.7%)	2 (9.1%)	20 (14.7%)
Non-Compliance with Study Drug	0	0	0	0	0
Death	0	0	0	1 (4.6%)	1 (0.7%)
Other	1 (2.2%)	0	1 (4.4%)	0	2 (1.5%)

Percent Change in Body Weight from Baseline at Week 26 (mITT)

	Placebo	Nimacimab 200 mg	Placebo + Semaglutide	Nimacimab 200 mg + Semaglutide
	n=44	n=40	n=24	n=28
Mean % Change from baseline (SD)	0.16 (5.394)	-1.05 (4.855)	-10.06 (6.216)	13.10 (7.108)
Least-squares mean percent reduction (SE)* (95% CI)	-0.26 (0.881) (-2.0, 1.5)	-1.52 (0.889) (-3.3, 0.2)	-10.25 (1.092) (-12.4, -8.1)	-13.2 (1.016) (-15.2, -11.2)
Placebo-subtracted weight loss (SE) (95% CI), P-value		-1.26 (1.136) (-3.5, 1.0), 0.2699	-9.99 (1.286) (-12.5, -7.4), <0.0001	-12.94 (1.244) (-15.4, -10.5), <0.0001
Semaglutide-subtracted weight loss (SE) (95% CI), P-value				**-2.95 (1.405) (-5.7, -0.2), 0.0372**

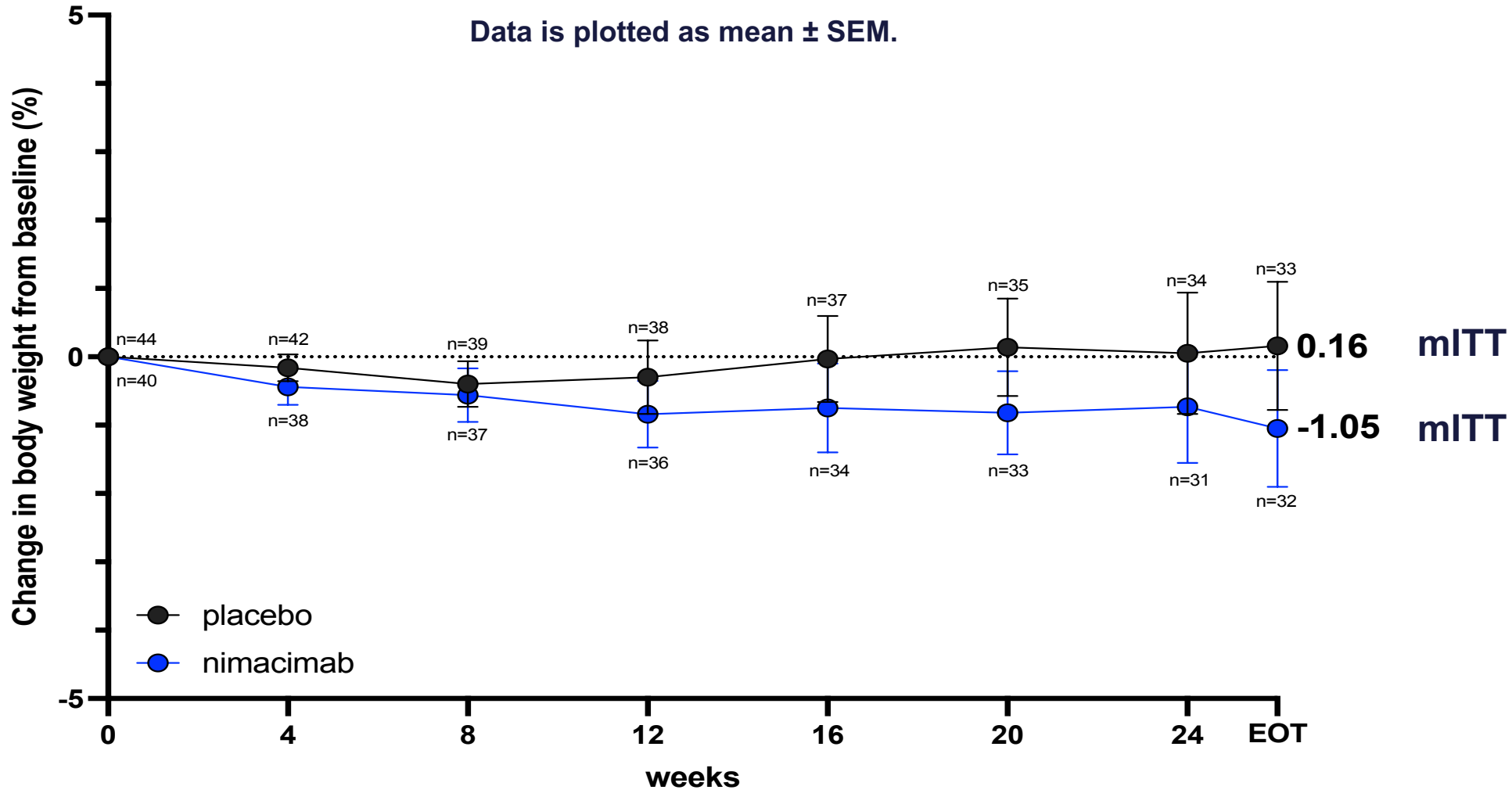
SE = Standard Error, CI = Confidence Interval
mITT = Modified Intent to Treat includes all participants who are randomized and who receive any amount of study medication regardless of adherence to the treatment plan

Percent Change in Body Weight from Baseline at Week 26 (Per Protocol)

	Placebo	Nimacimab 200 mg	Placebo + Semaglutide	Nimacimab 200 mg + Semaglutide
	n=28	n=29	n=20	n=21
Mean % Change from baseline (SD)	0.53 (5.631)	-0.44 (4.338)	-10.38 (6.200)	-13.65 (6.778)
Least-squares mean percent reduction (SE)* (95% CI)	0.81 (1.013) (-1.2, 2.8)	-0.52 (0.936) (-2.4, 1.3)	-9.97 (1.143) (-12.2, -7.7)	-13.47 (1.087) (-15.6, -11.3)
Placebo-subtracted weight loss (SE) (95% CI), P-value		-1.33 (1.246) (-3.8, 1.1), 0.2878	-10.78 (1.365) (-13.5, -8.1), <0.0001	-14.29 (1.334) (-16.9, -11.6), <0.0001
Semaglutide-subtracted weight loss (SE) (95% CI), P-value				**-3.51 (1.460) (-6.4, -0.6), 0.0178**

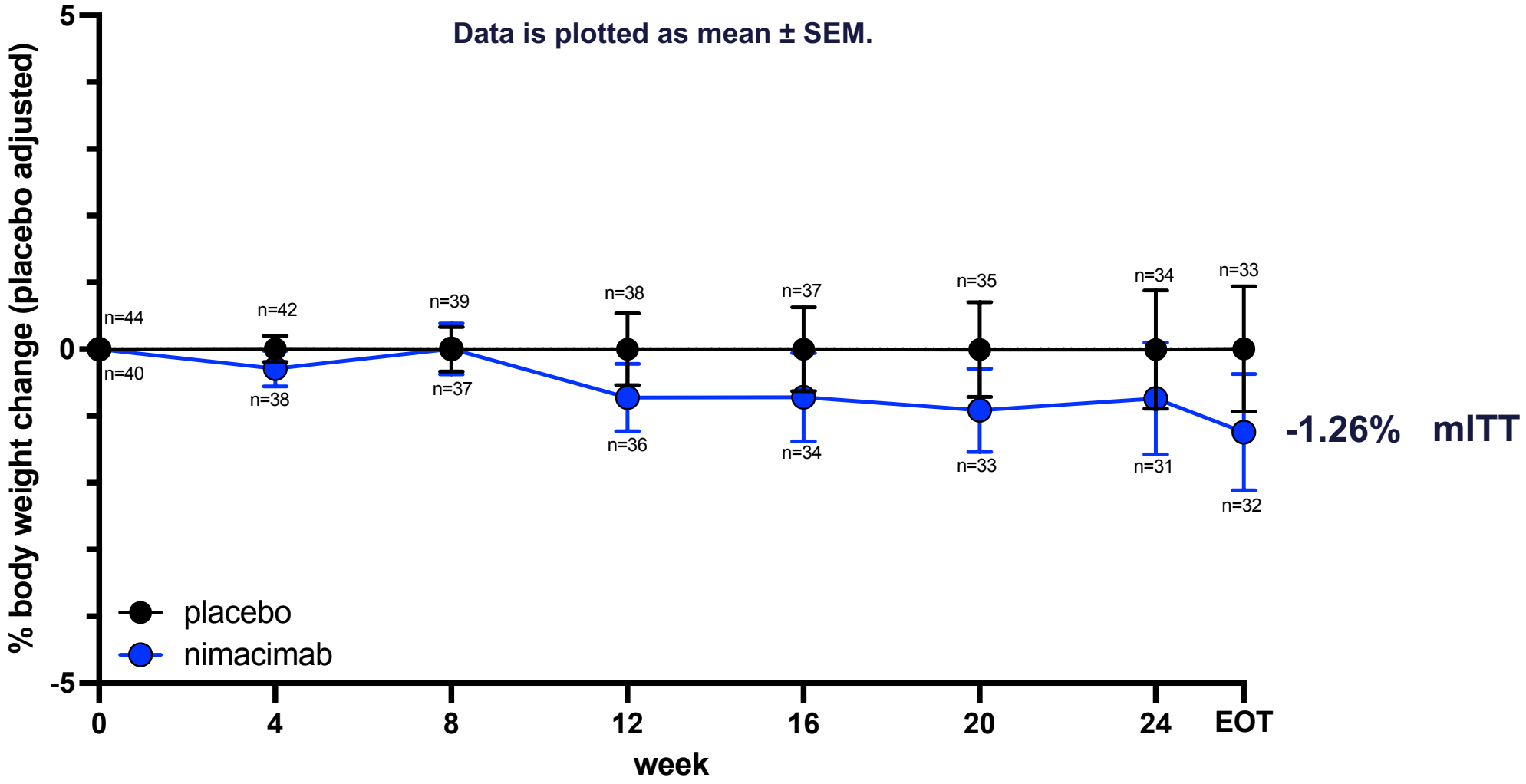
SE = Standard Error, LS = Least Squares, CI = Confidence Interval
PP = Per Protocol excludes major protocol deviations and non-adherent subjects

Weight Loss with Nimacimab Treatment



PP change in body weight from baseline placebo: 0.53
PP change in body weight from baseline nimacimab: -0.44

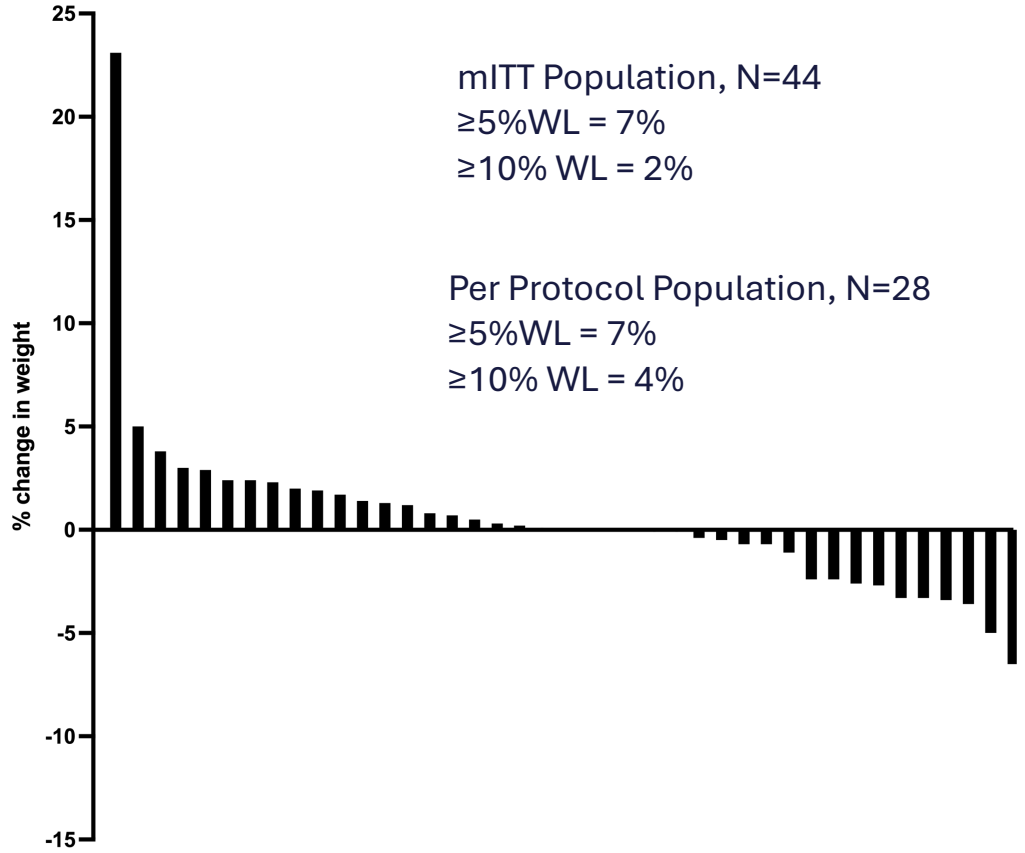
Placebo-Adjusted Weight Loss with Nimacimab Treatment



mITT LS Mean Difference: -1.26 (1.136); CI (-3.5, 1.0); p = 0.2699
PP LS Mean Difference: -1.33 (1.246); CI (-3.8, 1.1); p=0.2578

Weight Loss by Subject: Placebo v. Nimacimab Week 26

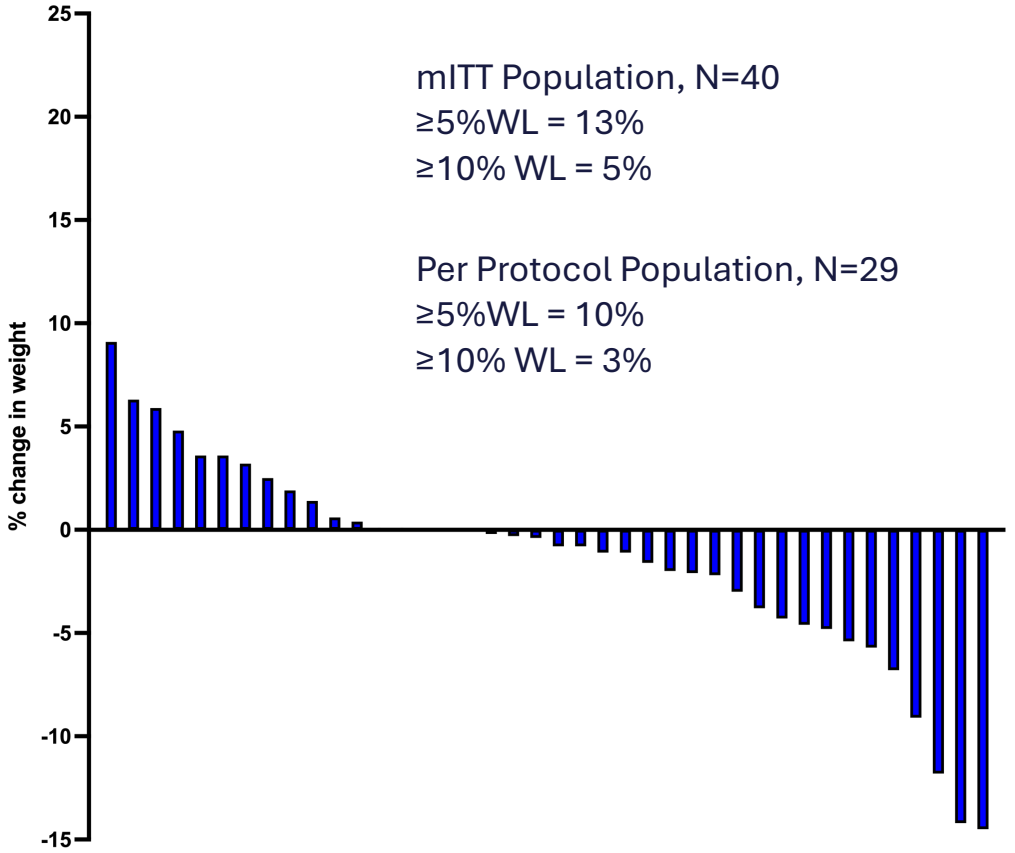
Placebo



mITT Population, N=44
≥5%WL = 7%
≥10% WL = 2%

Per Protocol Population, N=28
≥5%WL = 7%
≥10% WL = 4%

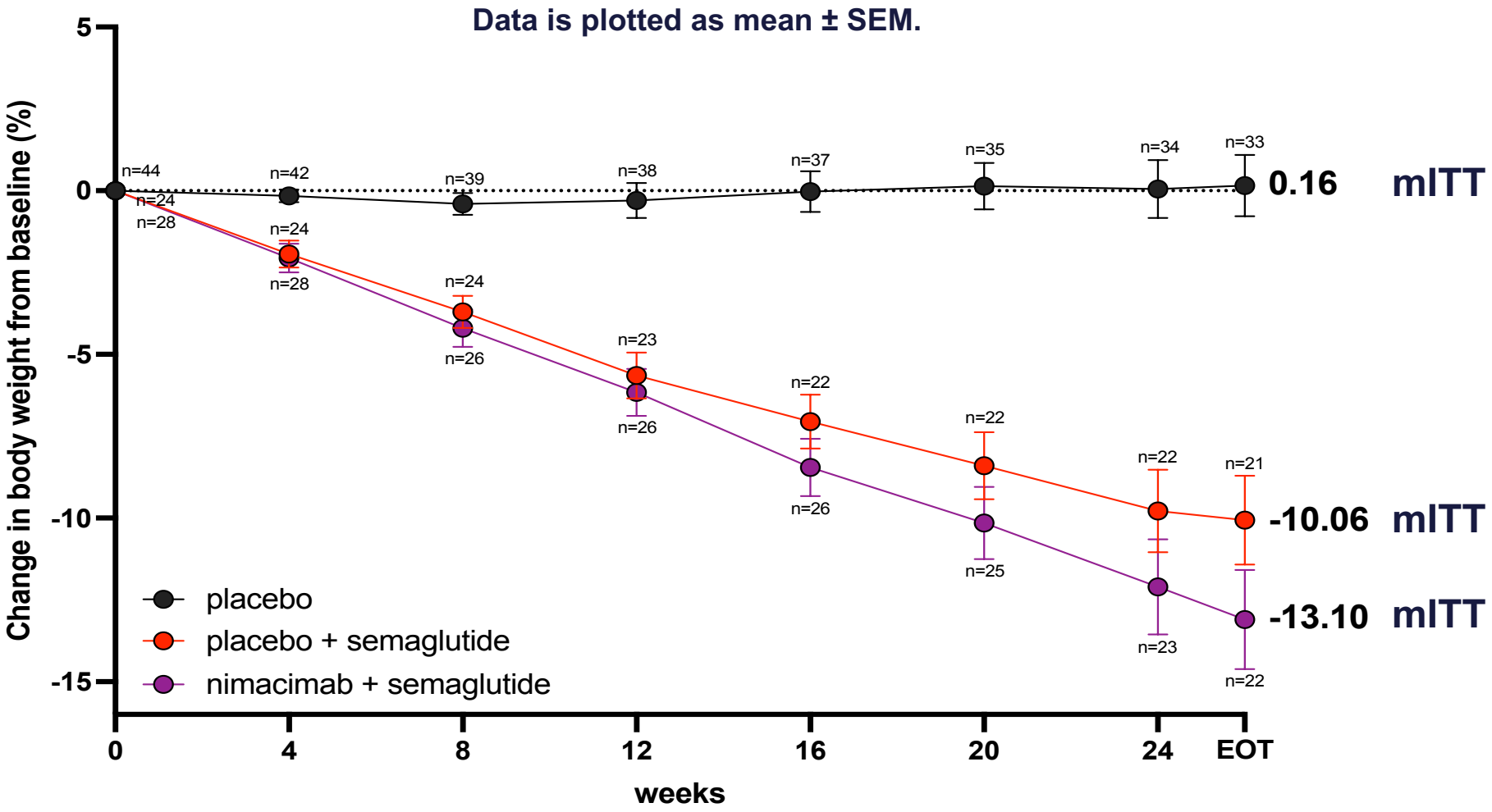
Nimacimab



mITT Population, N=40
≥5%WL = 13%
≥10% WL = 5%

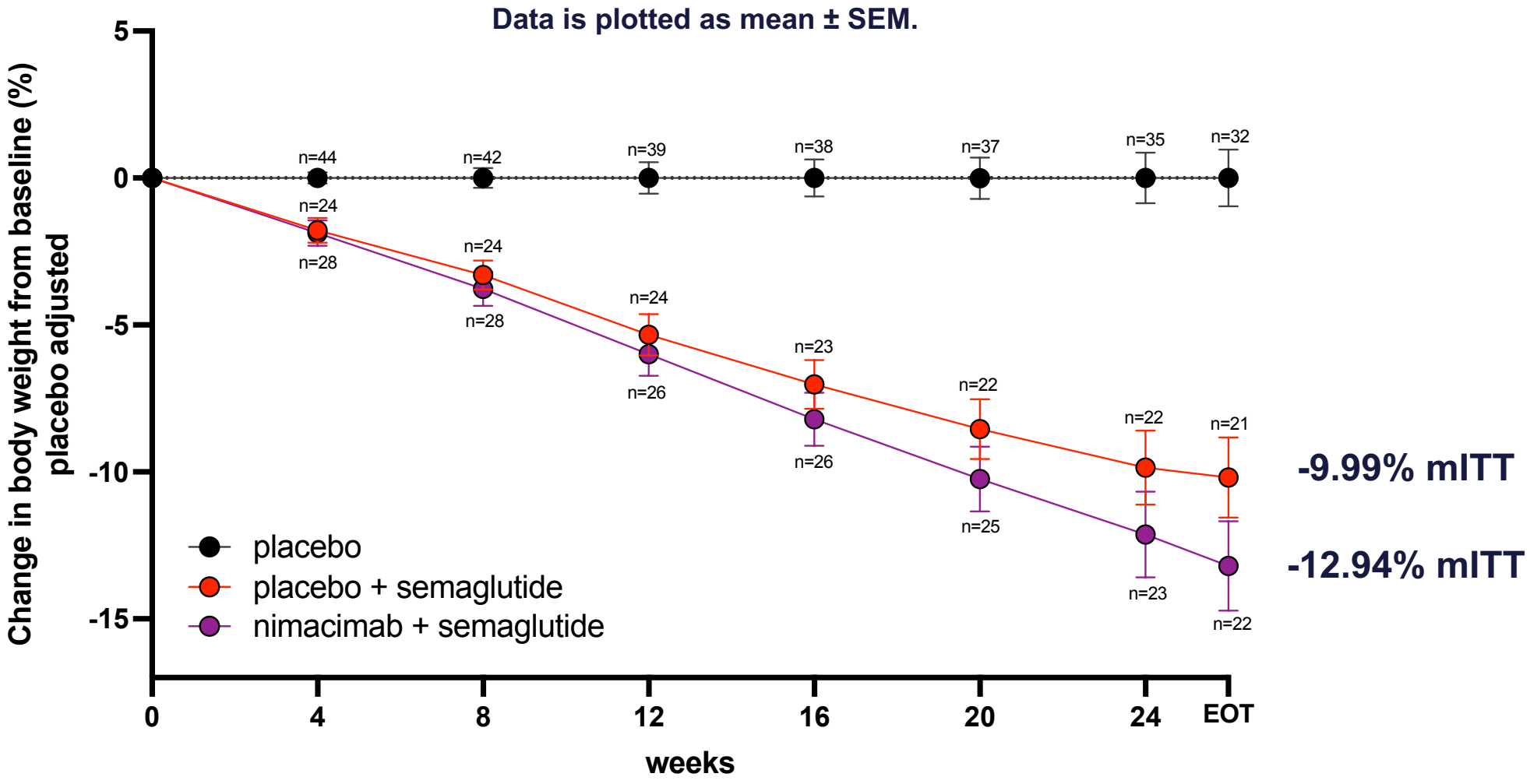
Per Protocol Population, N=29
≥5%WL = 10%
≥10% WL = 3%

Increased Weight Loss in Combination-Treated Patients



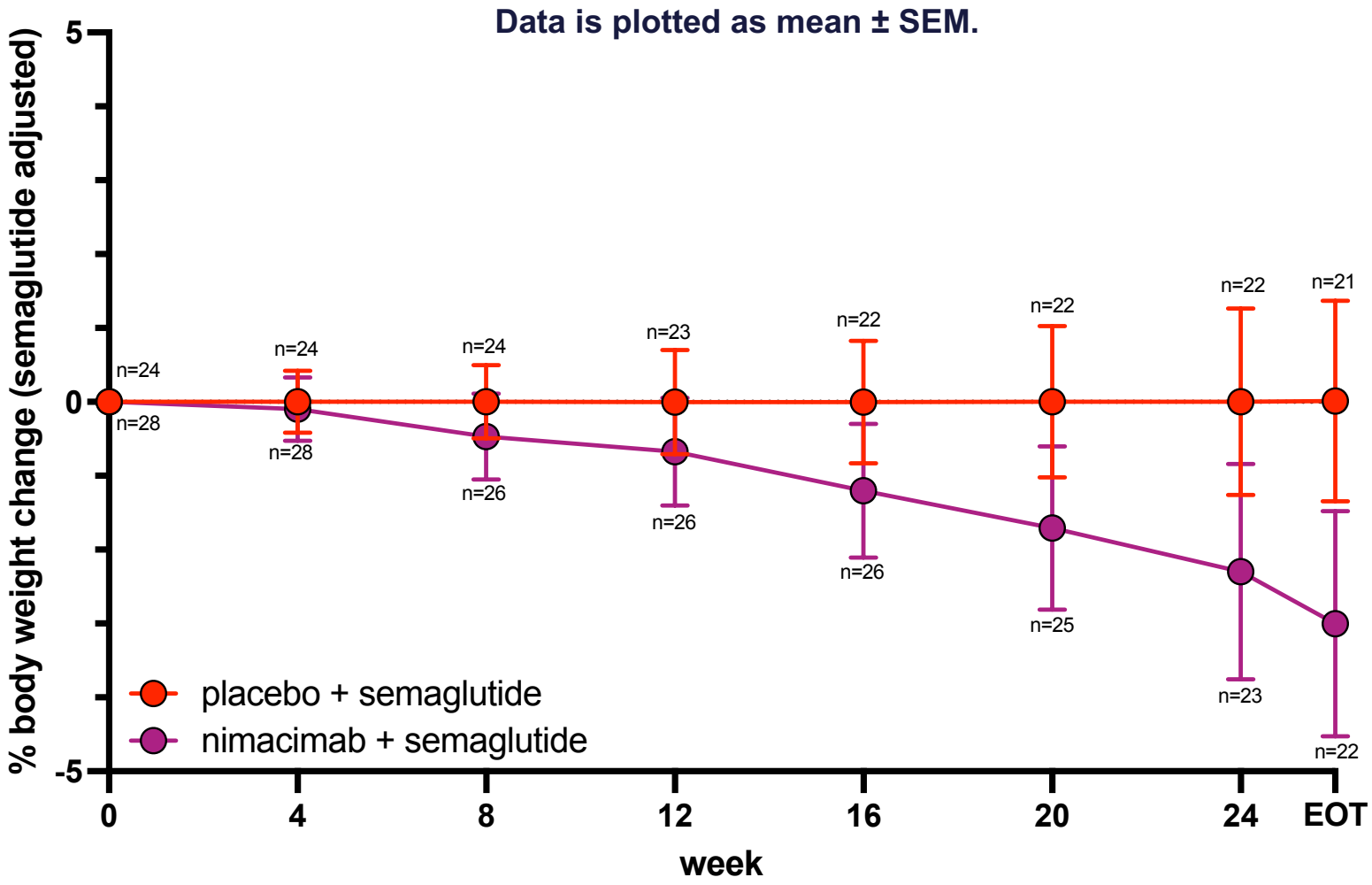
PP change in body weight from baseline placebo + semaglutide: -10.38
PP change in body weight from baseline nimacimab + semaglutide: -13.65

Increased Weight Loss in Combination–Treated Patients



mITT LS Mean Difference: -2.95 (1.405) (-5.7, -0.2), 0.0372
PP LS Mean Difference: -3.51 (1.460) (-6.4, -0.6), 0.0178

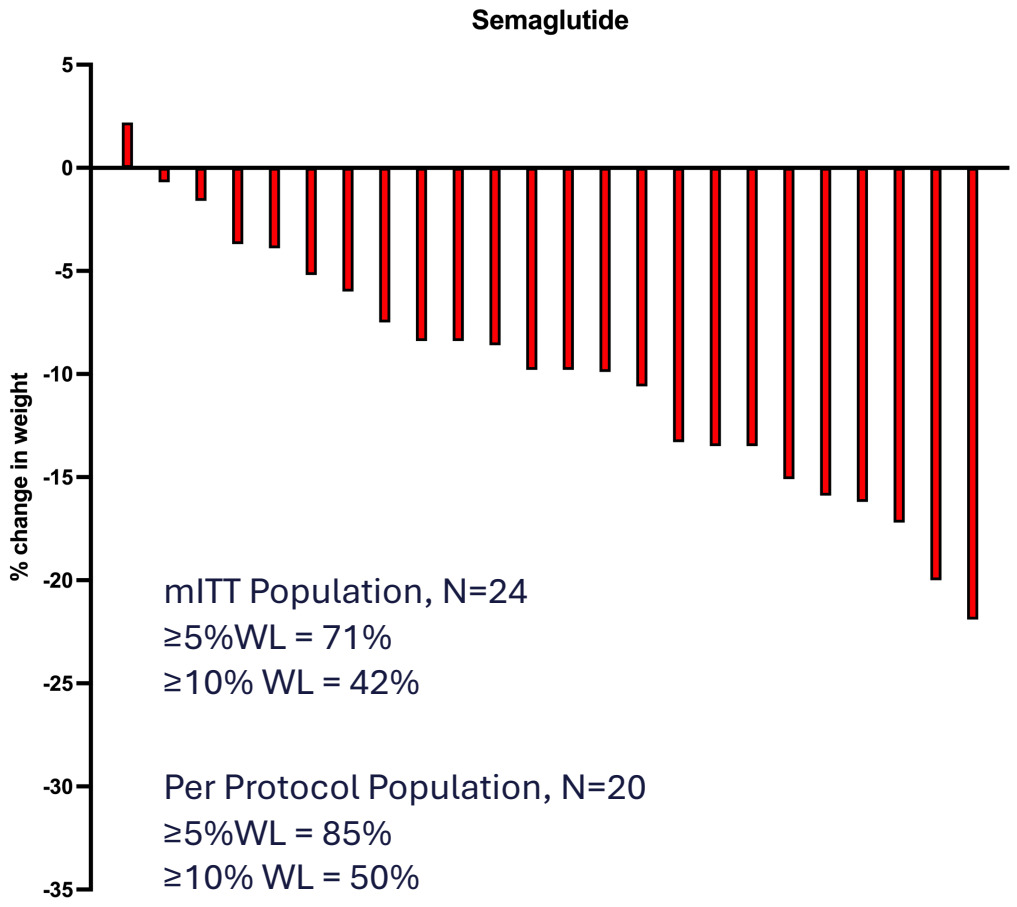
Semaglutide–Adjusted Weight Loss with Combo Treatment



-2.95% mITT

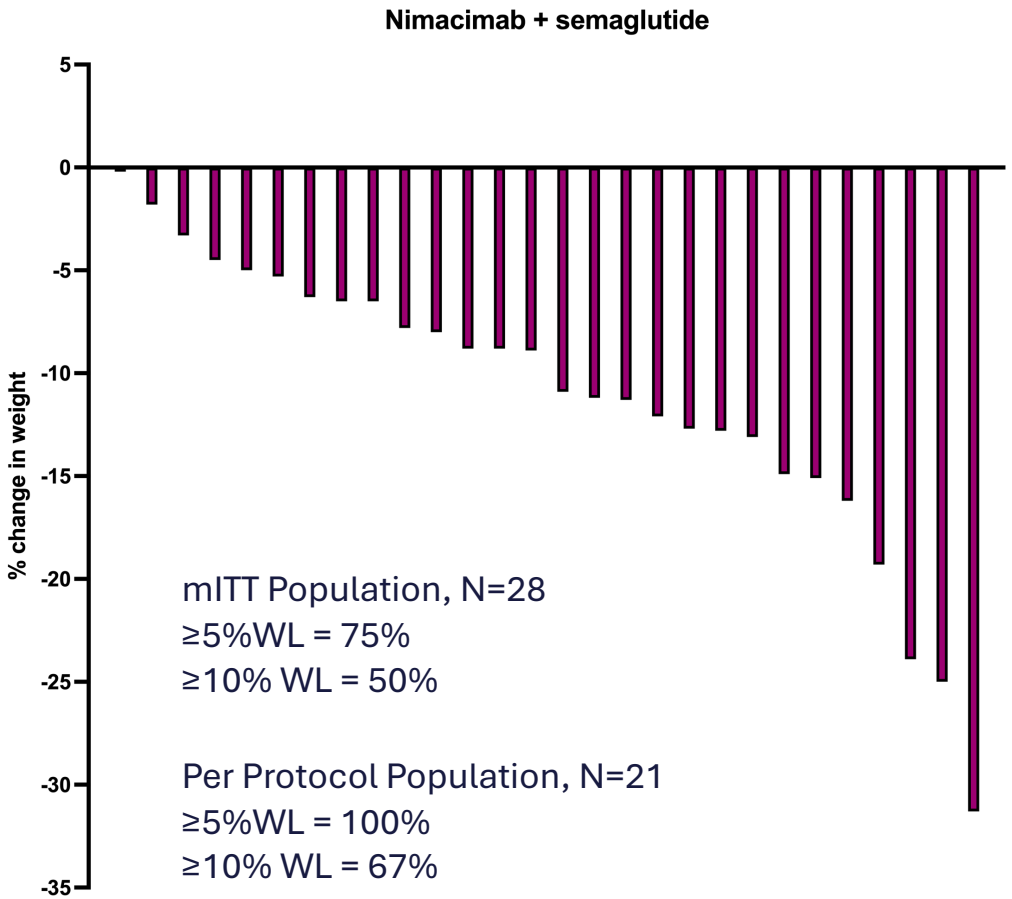
mITT LS Mean Difference: -2.95 (1.405) (-5.7, -0.2), 0.0372
PP LS Mean Difference: -3.51 (1.460) (-6.4, -0.6), 0.0178

Weight Loss by Subject: Semaglutide v. Combination Week 26



mITT Population, N=24
≥5%WL = 71%
≥10% WL = 42%

Per Protocol Population, N=20
≥5%WL = 85%
≥10% WL = 50%

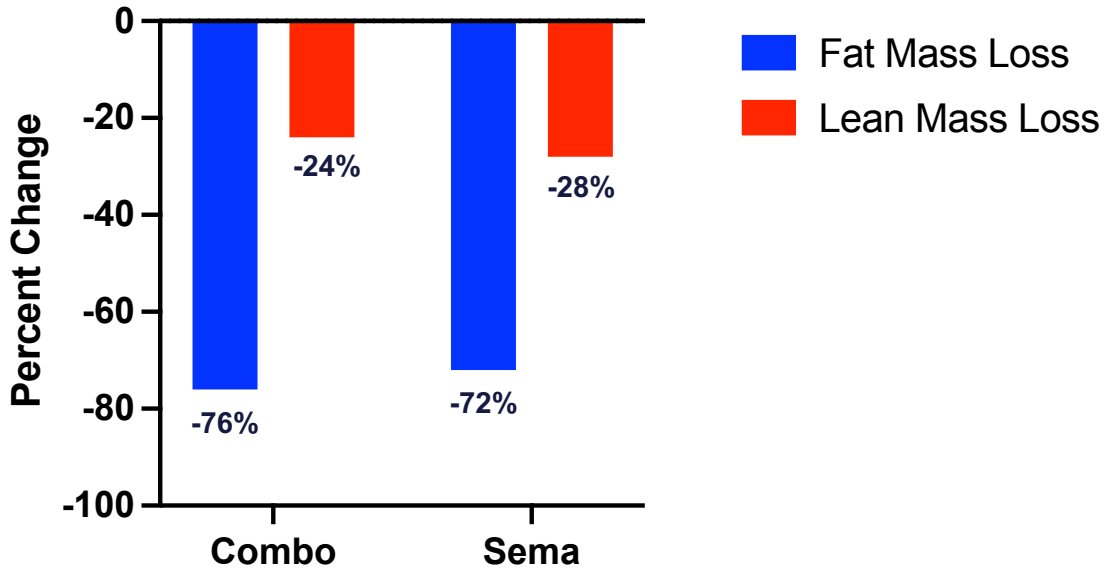


mITT Population, N=28
≥5%WL = 75%
≥10% WL = 50%

Per Protocol Population, N=21
≥5%WL = 100%
≥10% WL = 67%

DEXA: Nimacimab Plus Semaglutide Improves Body Composition

Baseline vs Week 26
Lean Mass vs. Fat Mass Loss

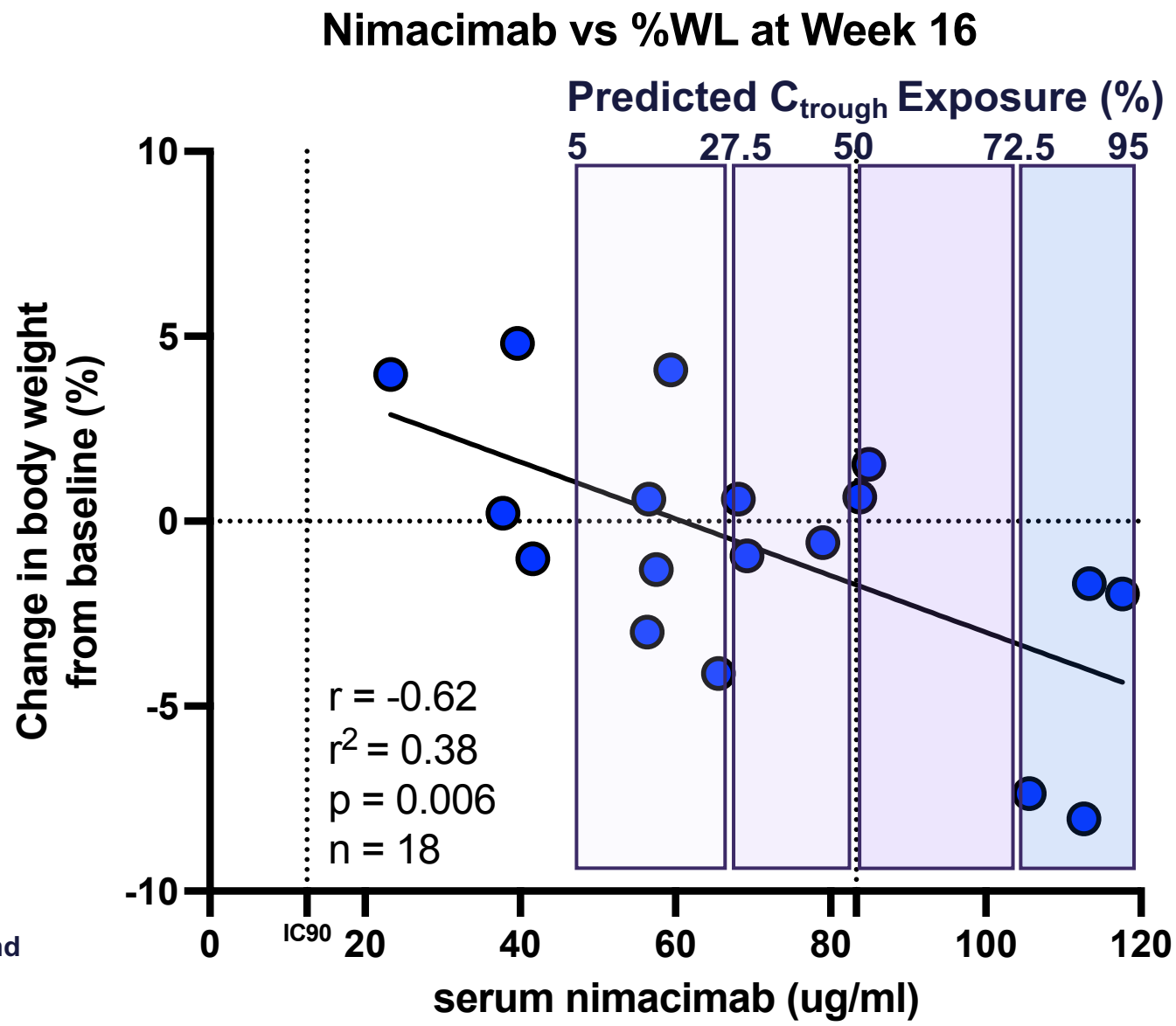


Change in Lean to Fat Mass Ratio with weight loss

	Placebo + Semaglutide	Nimacimab 200 mg + Semaglutide
	n=20	n=25
Mean baseline lean to fat mass ratio (SD)	1.15 (0.296)	1.06 (0.216)
Mean Week 26 lean to fat mass ratio (SD)	1.32 (0.312)	1.30 (0.463)
Least-squares mean change from baseline (SE)* (95% CI)	0.13 (0.038) (0.1, 0.2)	0.26 (0.037) (0.2, 0.3)
Least-squares mean difference from semaglutide (SE) (95% CI), P-value		**0.13 (0.051) (0.0, 0.2), p= 0.0126**

The addition of nimacimab increases weight loss from semaglutide while reducing the loss of lean mass and improving the lean/fat mass ratio

Association of Weight Loss and Exposure of Nimacimab



Removed (1) patient who discontinued nimacimab and switched to tirzepatide therapy at week 12

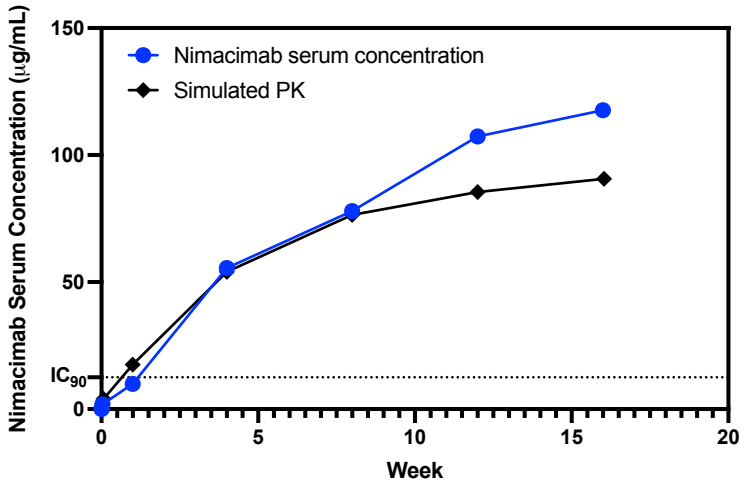
Preliminary PK Curves Highlight Inconsistent Exposure

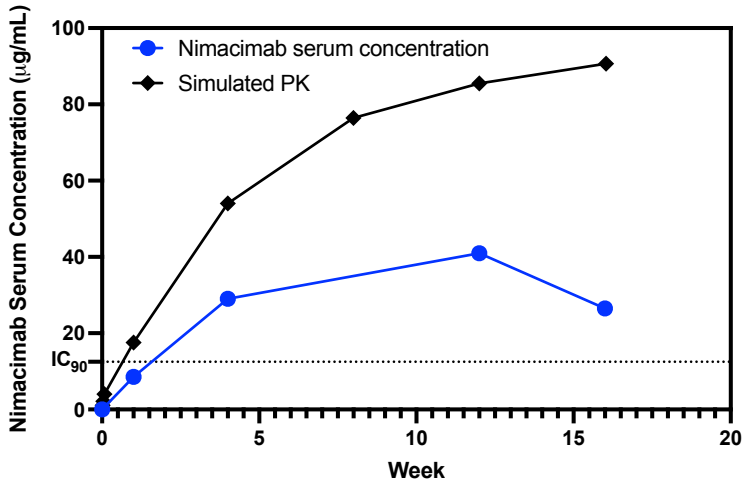
Initial Anti-Drug Antibody (ADA) analysis suggests that ADA is not driving nimacimab clearance

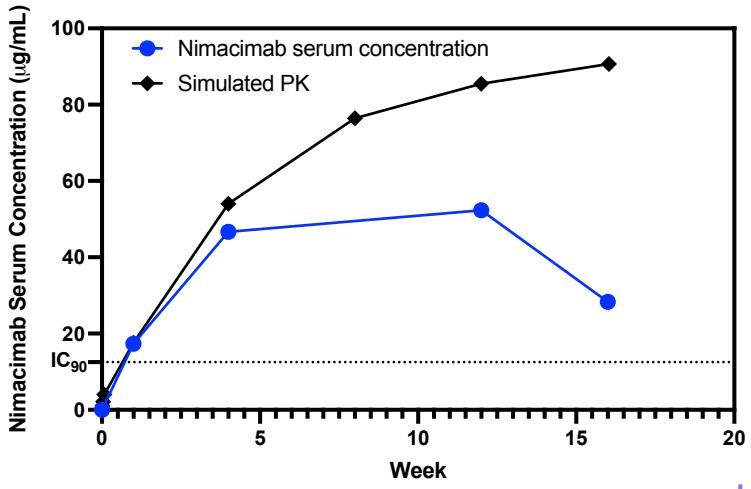
The majority of patients had PK curves below the predicted exposure through Week 16

Observed in both monotherapy and combination cohorts

Examples of PK Curves (C_{trough}) through Week 16







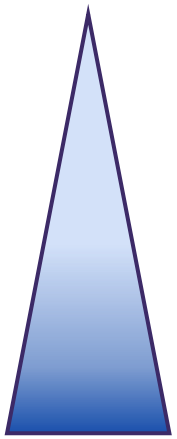
Expected PK Behavior

Sub-optimal PK

DIO Studies Demonstrate a Wide and Effective Dose Range

Clinical translation of nimacimab exposure in the CBeyond trial highlights the potential for greater weight loss with a higher dose

Nimacimab Dose	pAUC h*ug/mL	Weight Change (%) 24-day mouse DIO	Relative Efficacy
7.5 mg/kg Q3D	103,278	- 2.3	
24 mg/kg Q3D	330,490	- 9.5	
75 mg/kg Q3D	1,032,780	- (13-17)	
240 mg/kg Q3D	3,304,900	- (17-22)	
750 mg/kg Q3D	10,327,800	- 24	



← CBeyond Clinical Dose*

* 200 mg SC QW: preliminary average AUC at 26 weeks = 243,013 h*ug/mL

CBeyond Safety and Tolerability

Reported TEAEs by Severity

Max Severity	Nimacimab 200 mg	Placebo	Nimacimab 200 mg + Semaglutide	Placebo + Semaglutide	Overall
	n=40	n=44	n=28	n=24	n=136
Mild	20 (50.0%), 174	14 (31.8%), 109	11 (39.3%), 80	10 (41.7%), 113	55 (40.4%), 476
Moderate	11 (27.5%), 18	17 (38.6%), 34	11 (39.3%), 25	10 (41.7%), 24	49 (36.0%), 101
Severe	2 (5.0%), 3	2 (4.5%), 3	0, 0	2 (8.3%), 2	6 (4.4%), 8
Missing	0, 0	0, 0	0, 0	0, 0	0, 0
Total	33 (82.5%), 195	33 (75.0%), 146	22 (78.6%), 105	22 (91.7%), 139	110 (80.9%), 585

TEAEs by System Organ Class

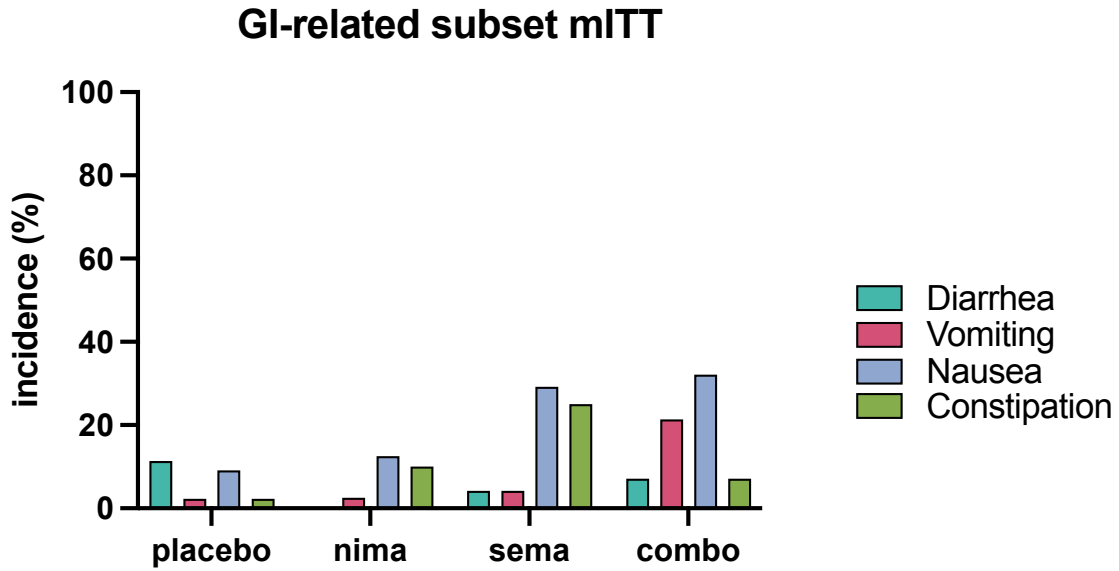
System Organ Class	Nimacimab 200 mg	Placebo	Nimacimab 200 mg + Semaglutide	Placebo + Semaglutide	Overall
	n=40	n=44	n=28	n=24	n=136
General disorders and administration site conditions	16 (40.0%), 101	14 (31.8%), 33	7 (25.0%), 12	11 (45.8%), 39	48 (35.3%), 185
Infections and Infestations	13 (32.5%), 17	13 (29.5%), 15	10 (35.7%), 14	9 (37.5%), 14	45 (33.1%), 60
Gastrointestinal disorders	11 (27.5%), 19	13 (29.5%), 20	16 (57.1%), 37	16 (66.7%), 37	56 (41.2%), 113
Nervous system disorders	10 (25.0%), 20	15 (34.1%), 21	10 (35.7%), 18	9 (37.5%), 11	44 (32.4%), 70
Metabolism and nutrition disorders	8 (20.0%), 8	3 (6.8%), 3	4 (14.3%), 6	1 (4.2%), 2	16 (11.8%), 19
Investigations	7 (17.5%), 9	4 (9.1%), 10	1 (3.6%), 1	3 (12.5%), 6	15 (11.0%), 26

Most Reported TEAEs by Preferred Term

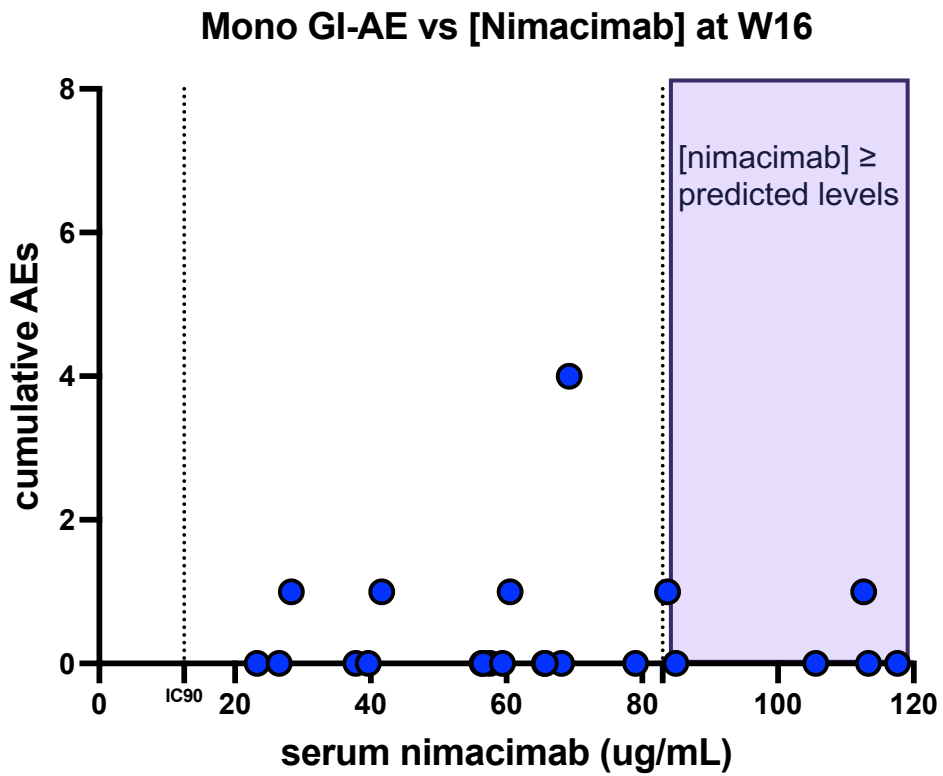
Preferred Term	Nimacimab 200 mg	Placebo	Nimacimab 200 mg + Semaglutide	Placebo + Semaglutide	Overall
	n=40	n=44	n=28	n=24	n=136
Injection site erythema	7 (17.5%), 50	6 (13.6%), 12	2 (7.1%), 3	3 (12.5%) 15	18 (13.2%), 80
Nausea	5 (12.5%), 6	4 (9.1%), 4	9 (32.1%), 12	7 (29.2%), 7	25 (18.4%), 29
Headache	5 (12.5%), 6	3 (6.8%), 4	3 (10.7%), 3	3 (12.5%), 4	14 (10.3%), 17
Injection site reaction	5 (12.5%), 21	2 (4.5%), 3	1 (3.6%), 2	1 (4.2%), 2	9 (6.6%), 28
Constipation	4 (10.0%), 4	1 (2.3%), 1	2 (7.1%), 2	6 (25.0%), 7	13 (9.6%), 14
Upper respiratory tract infection	4 (10.0%), 5	1 (2.3%), 1	1 (3.6%), 1	2 (8.3%), 3	8 (5.9%), 10
Dizziness	3 (7.5%), 5	7 (15.9%), 7	5 (17.9%), 5	6 (25.0%), 6	21 (15.4%), 23
Decreased appetite	3 (7.5%), 3	1 (2.3%), 1	3 (10.7%), 3	1 (4.2%), 1	8 (5.9%), 8
Injection site bruising	3 (7.5%), 6	5 (11.4%), 8	2 (7.1%), 2	3 (12.5%), 4	13 (9.6%), 20
Injection site pain	3 (7.5%), 4	1 (2.3%), 1	0, 0	2 (8.3%), 6	6 (4.4%), 11
Vomiting	1 (2.5%), 1	1 (2.3%), 1	6 (21.4%), 8	1 (4.2%), 1	9 (6.6%), 11
Diarrhea	0, 0	5 (11.4%), 6	2 (7.1%), 4	1 (4.2%), 1	8 (5.9%), 11

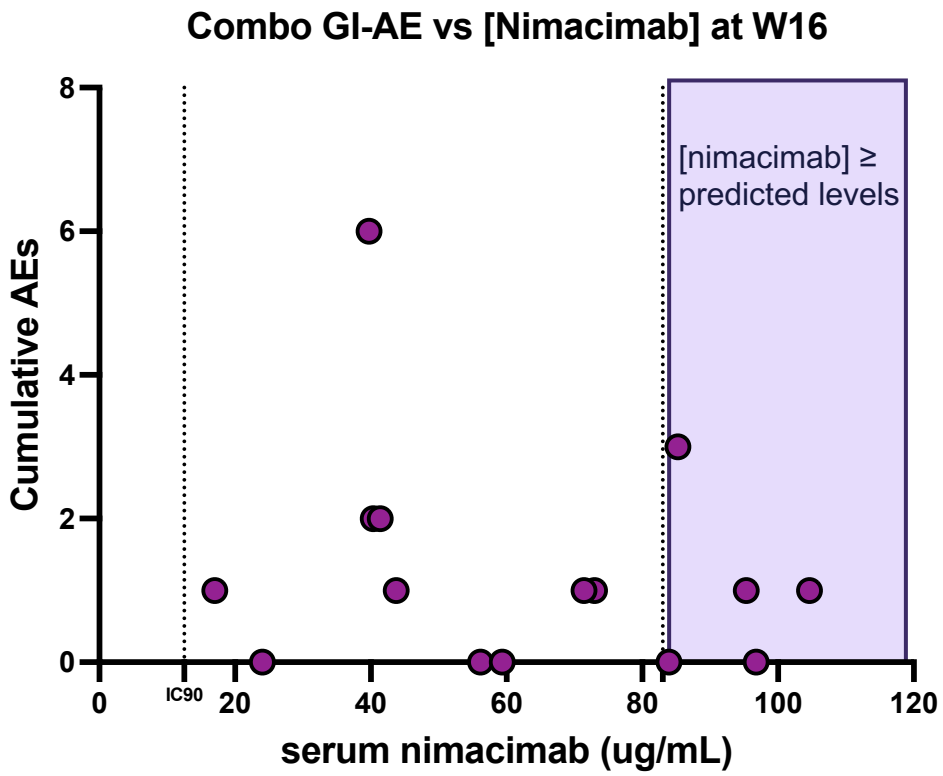
Gastrointestinal Disorders

Max Severity	Nimacimab 200 mg	Placebo	Nimacimab 200 mg + Semaglutide	Placebo + Semaglutide	Overall
	n=40	n=44	n=28	n=24	n=136
Mild	8 (20.0%), 16	8 (18.2%), 15	11 (39.3%), 27	11 (45.8%), 32	38 (27.9%), 90
Moderate	3 (7.5%), 3	5 (11.4%), 5	5 (17.9%), 10	5 (20.8%), 5	18 (13.2%), 23
Severe	0, 0	0, 0	0, 0	0, 0	0, 0
Missing	0, 0	0, 0	0, 0	0, 0	0, 0
Total	11 (27.5%), 19	13 (29.5%), 20	16 (57.1%), 37	16 (66.7%), 37	56 (41.2%), 113



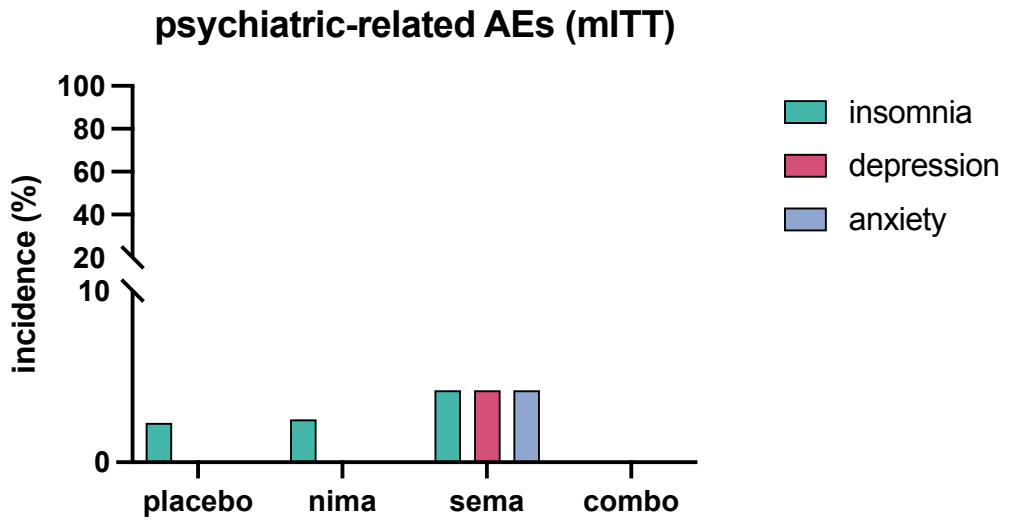
Higher Nimacimab Concentration Was Not Associated with GI–AEs





Psychiatric Disorders

Max Severity	Nimacimab 200 mg	Placebo	Nimacimab 200 mg + Semaglutide	Placebo + Semaglutide	Overall
	n=40	n=44	n=28	n=24	n=136
Mild	1 (2.5%), 1	1 (2.3%), 1	0, 0	1 (4.2%), 2	3 (2.2%), 4
Moderate	0, 0	0.0	0, 0	1 (4.2%), 1	1 (0.7%), 1
Severe	0, 0	0, 0	0, 0	0, 0	0, 0
Missing	0, 0	0, 0	0, 0	0, 0	0, 0
Total	1 (2.5%), 1	1 (2.3%), 1	0.0	2 (8.3%), 3	4 (2.9%), 5



4 patients reported psychiatric-related AEs
(insomnia n=3 events, anxiety n=1 events, depression n=1 events)

CBeyond Summary and the Path Forward

Summary and the Path Forward

Key Results

- **Monotherapy (200 mg QW):** Did not meet primary endpoint; placebo-adjusted weight loss at 26 weeks was -1.26%, p=0.2699, mITT and -1.33%, p=0.2878, PP.
- **Combination with Semaglutide:** Achieved a clinically meaningful placebo-adjusted weight loss vs semaglutide alone (-12.9% vs -10.0%, p=0.0372, mITT and -14.3% vs -10.8%, p=0.0178, PP). Improved lean to fat mass ratio (0.26 vs. 0.13, p = 0.0126).
- **Safety & Tolerability:** Clean profile with no neuropsychiatric events and no added GI burden in the combination arm.

Interpretation

- **Underexposure:** Monotherapy effect limited at 200 mg, but exposure modeling and preclinical data suggest potential at higher doses.
- **Combo Arm Positive:** Combination data demonstrated additive efficacy with semaglutide and may support advancement as a potential differentiated, combination-ready therapy.
- **Safety Foundation of TPP Intact:** No increased safety burden at 200 mg dose; higher exposure not linked to increased AEs.

Next Steps

- **Evaluate Exposure/Response** → Continue to evaluate data to determine next steps, including potential future clinical studies to confirm optimal exposure and regimen.
- **Leverage Combo Opportunity** → Focus on combination strategy while continuing to evaluate higher-dose monotherapy.
- **Monotherapy Development** → Assessing a path for a monotherapy maintenance setting.
- **Build on Clean Safety** → Advance with confidence; nimacimab has not been observed to add to the GLP-1 gastrointestinal AE profile to date, and no neuropsychiatric AEs have been observed, reinforcing the potential differentiated safety of peripheral CB1 inhibition.

CBeyond Question & Answer Session