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REDEFINE 1: Effect of CagriSema 2.4 mg/2.4 mg on body composition, muscle strength and physical function

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Presenter disclosure

- Eric Ravussin reports the following:
  - Receiving grants or contracts from Eli Lilly, Boehringer Ingelheim, ICON, Novartis, Sanofi-Aventis, Novo Nordisk, Biolinq and Amgen; and consulting fees from Energesis Pharmaceuticals, Eli Lilly USA, Merck, Amway, Novo Nordisk, Altimmune, AbbVie, Amgen, OrbiMed, Boehringer Ingelheim and Structure Therapeutics

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Balancing weight loss and muscle preservation in obesity treatment

Preserving physical function and muscle strength is important during weight loss.[1] Substantial weight loss achieved via any means primarily reflects reductions in fat mass, with limited evidence of a significant loss in skeletal muscle mass[2,3]

In the global phase 3a REDEFINE 1 trial, CagriSema treatment resulted in a **mean weight loss of 22.7%†** compared to 2.3% with placebo[4]

In this analysis, changes in body composition and correlations with physical function and muscle strength were assessed in a subgroup of participants from REDEFINE 1 who had DXA scans

†Data from the trial-product estimand, which assessed the effects if the trial products were taken as intended (including any of the approved doses) and was based on data from the on-treatment period. DXA, dual-energy X-ray absorptiometry.

1. Sattar N et al. Lancet Diabetes 2025;13:482–493; 2. Grandl G, et al. Lancet Reg Health Eur 2024:47:101100;
3. Neeland IJ et al. Diabetes Obes Metab 2024;26(suppl 4):16–27; 4. Garvey WT et al. N Engl J Med 2025;393:635–647.

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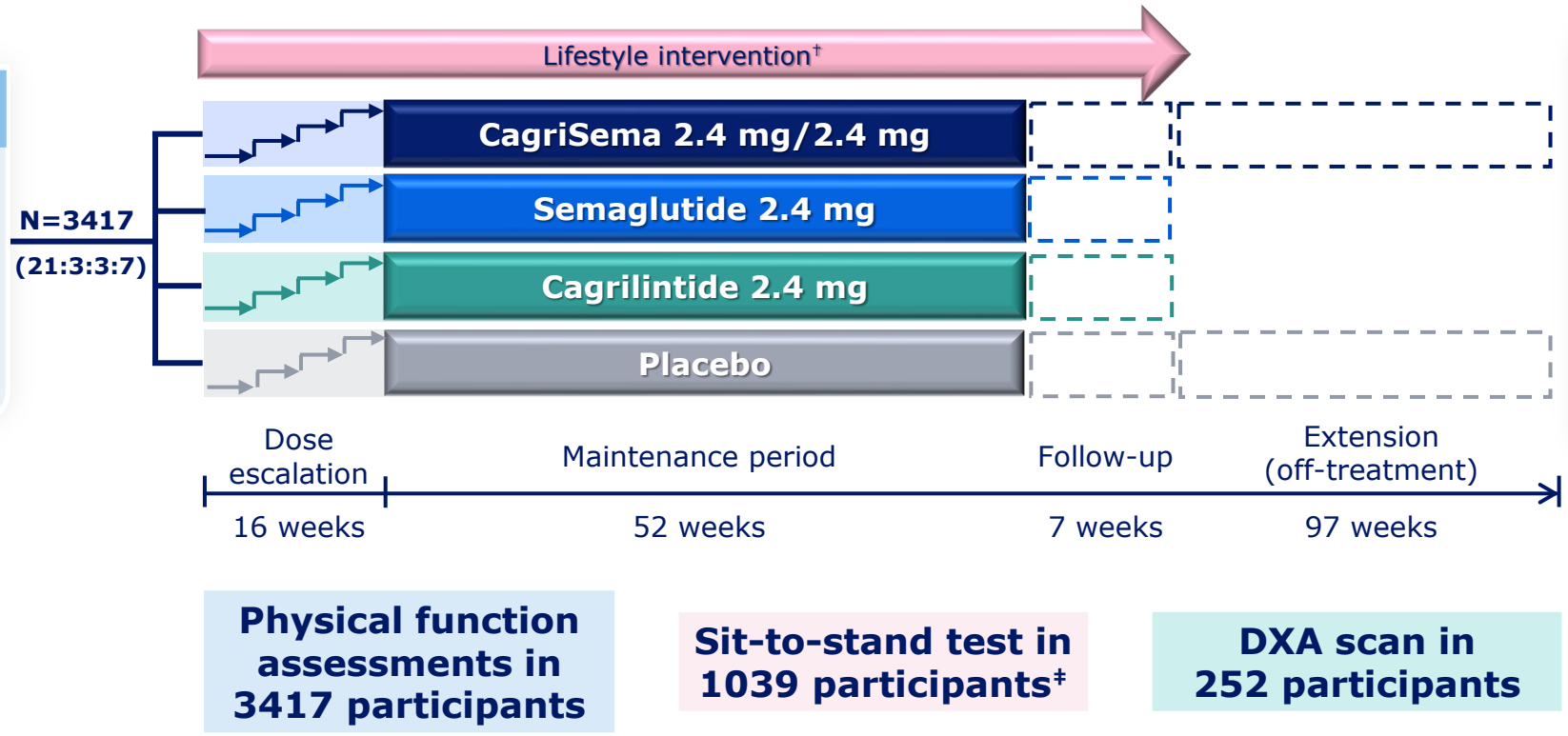
REDEFINE 1 was a 68-week, randomised, double-blind, placebo- and active-controlled, multicenter study

Inclusion criteria

- Male or female
- Aged ≥18 years
- BMI: ≥30 kg/m^2 or ≥27 kg/m^2 with ≥1 obesity-related complication



Physical function assessments in 3417 participants

Sit-to-stand test in 1039 participants‡

DXA scan in 252 participants

Key endpoints

Efficacy

Co-primary (vs placebo):

- Relative change in body weight (%) from baseline to 68 weeks
- Participants who achieve ≥5% body weight reduction from baseline to 68 weeks

†As an adjunct to a reduced-calorie diet and increased physical activity in adults with obesity or overweight during main phase only.
‡All participants in the DXA subgroup in Denmark, the Netherlands, Japan, UK and US performed a sit-to-stand test.
BMI, body mass index; DXA, dual-energy X-ray absorption. Illustration created by Novo Nordisk.
ClinicalTrials.gov NCT05567796. https://clinicaltrials.gov/study/NCT05567796 (accessed June 2025).

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Assessing body composition, physical function, and muscle strength in REDEFINE 1

Body composition assessed using DXA

- DXA can differentiate between bone mass, fat mass and lean soft tissue

Physical function assessed using patient-reported-outcomes

- IWQoL-Lite-CT Physical Function score (obesity-specific)
- SF36v2 Physical Functioning score

Muscle strength assessed using the sit-to-stand test

- The objective of the sit-to-stand test was to complete as many full sit-to-stand cycles as possible within 30 seconds

Study data presented using two estimands. Trial product estimand: the difference in mean change in body weight from baseline to week 68 for all randomised participants, had all participants remained on randomised treatment (regardless of dose level) without initiation of rescue intervention, in which trial product is used as adjunct to a reduced-calorie diet and increased physical activity. Treatment policy estimand: the difference in mean change in body weight from baseline to week 68 for all randomised participants, irrespective of adherence to treatment or initiation of anti-obesity rescue intervention, in which trial product is used as adjunct to a reduced-calorie diet and increased physical activity.
DXA, dual-energy X-ray absorptiometry; IWQoL-Lite-CT, Impact of Weight on Quality of Life-Lite Clinical Trials Version; SF-36v2, SF-36v2 Health Survey acute version.

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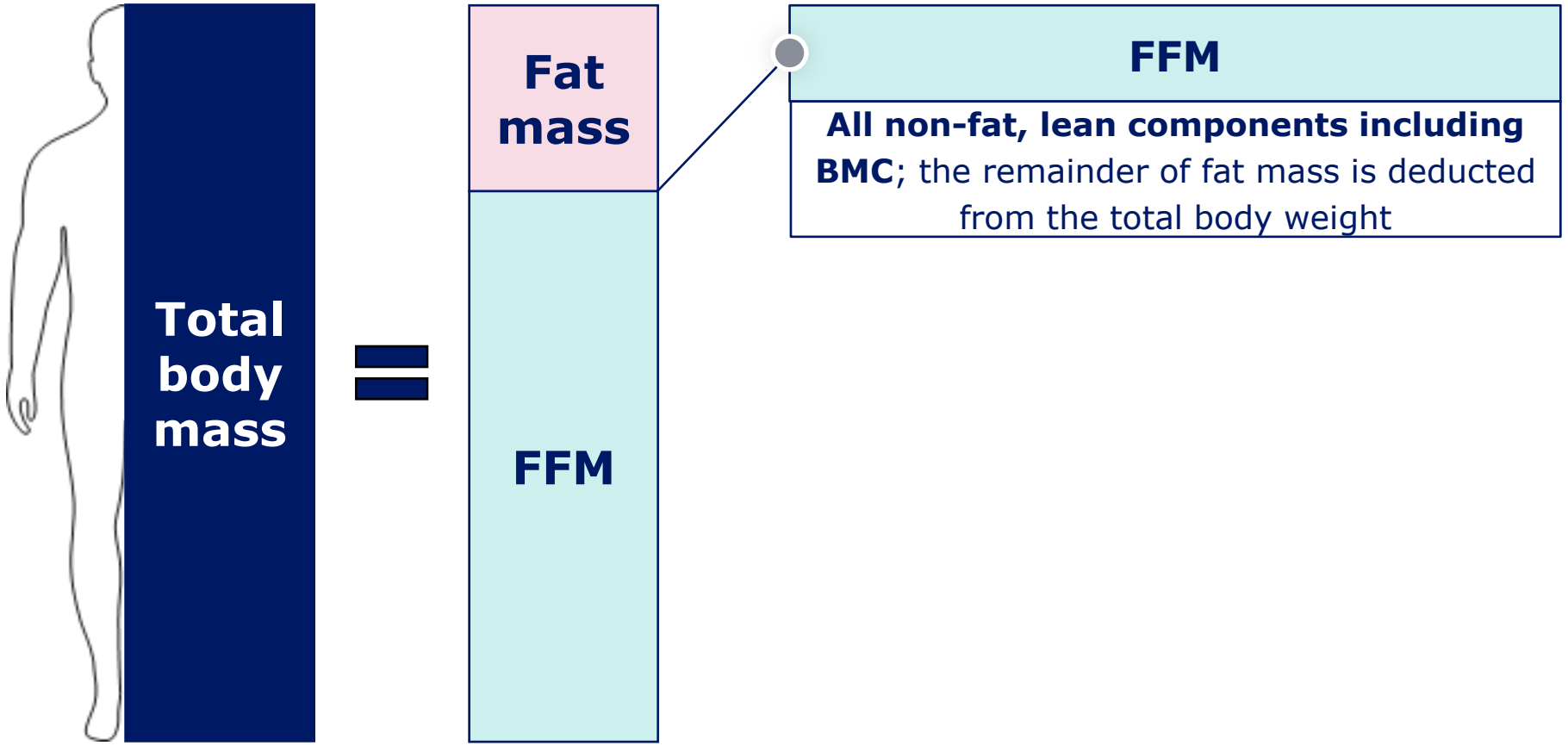
Interpreting FFM versus lean soft tissue from DXA



BMC, bone mineral content; DXA, dual X-ray absorptiometry; FFM, fat free mass.
Prado CM, et al. Am J Clin Nutr 2025;122:384-391.

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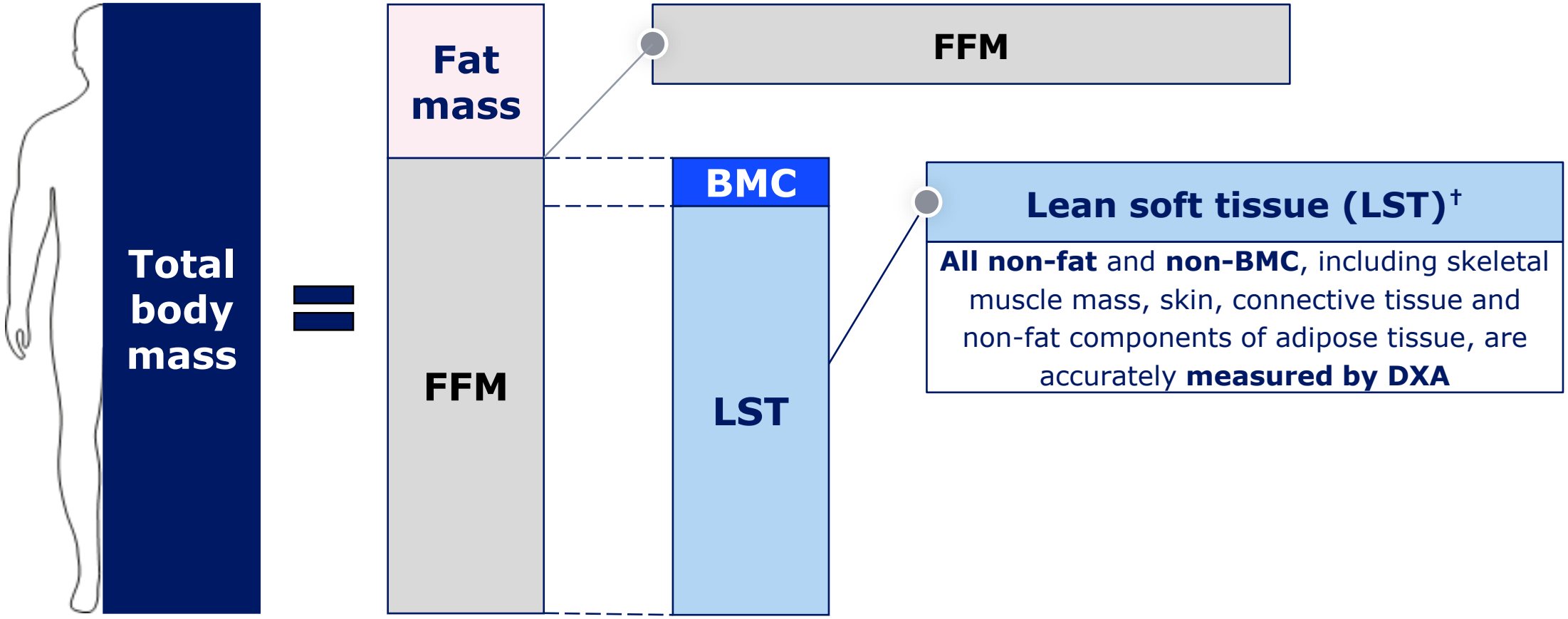

†Lean soft tissue should be reported to specify the non-inclusion of BMC. Lean soft tissue should not be confused with skeletal muscle mass.
BMC, bone mineral content; DXA, dual energy X-ray absorptiometry; FFM, fat free mass; LST, lean soft tissue.
Prado CM, et al. Am J Clin Nutr 2025;122:384-391.

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Baseline characteristics in the DXA subgroup

	CagriSema 2.4 mg/2.4 mg	Placebo
Number of participants	154	55
Age, years	50.1 (11.1)	48.7 (11.0)
Female sex, n (%)	113 (73.4)	42 (76.4)
Race, n (%)		
White	133 (86.4)	44 (80.0)
Asian	2 (1.3)	2 (3.6)
Black or African American	14 (9.1)	6 (10.9)
Other†	5 (3.2)	3 (5.5)
Body weight, kg	110.9 (19.1)	107.8 (18,7)
Height, m	1.7 (0.1)	1.7 (0.1)
BMI, kg/m²	38.7 (5.8)	38.1 (5.8)
Waist circumference, cm	116.8 (13.9)	113.0 (15.7)
Total fat mass, %	44.0 (6.9)	43.6 (7.9)
Lean soft tissue, %	53.6 (6.8)	53.9 (7.7)
Visceral fat mass, %	30.5 (9.5)	28.6 (7.8)

Data are mean (SD) unless otherwise stated. Mean, arithmetic mean.
†Other includes 'American Indian or Alaska Native', 'Native Hawaiian or other Pacific Islander', 'Multiple', 'Not reported', and 'Missing'.
BMI, body mass index; DXA, dual-energy X-ray absorptiometry; SD, standard deviation.

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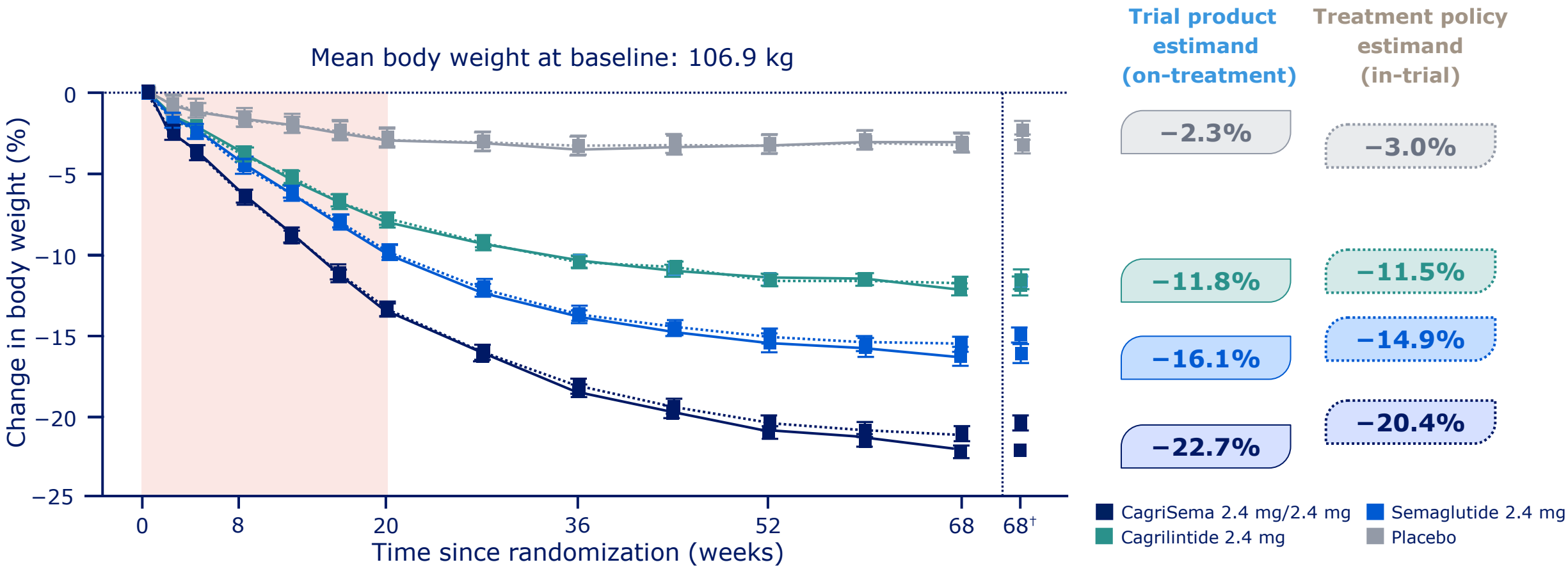
CagriSema 2.4 mg/2.4 mg demonstrated the greatest body weight reduction at week 68



Trial product estimand: The difference in mean change in body weight from baseline to week 68 for all randomised participants, had all participants remained on randomised treatment (regardless of dose level) without initiation of rescue intervention, in which trial product is used as adjunct to a reduced-calorie diet and increased physical activity. Treatment policy estimand: The difference in mean change in body weight from baseline to week 68 for all randomised participants, irrespective of adherence to treatment or initiation of anti-obesity rescue intervention, in which trial product is used as adjunct to a reduced-calorie diet and increased physical activity. Error bars are ± standard error of the mean. Illustration created by Novo Nordisk. Garvey WT et al. N Engl J Med 2025;393:635–647. †Estimated means from the statistical analysis.

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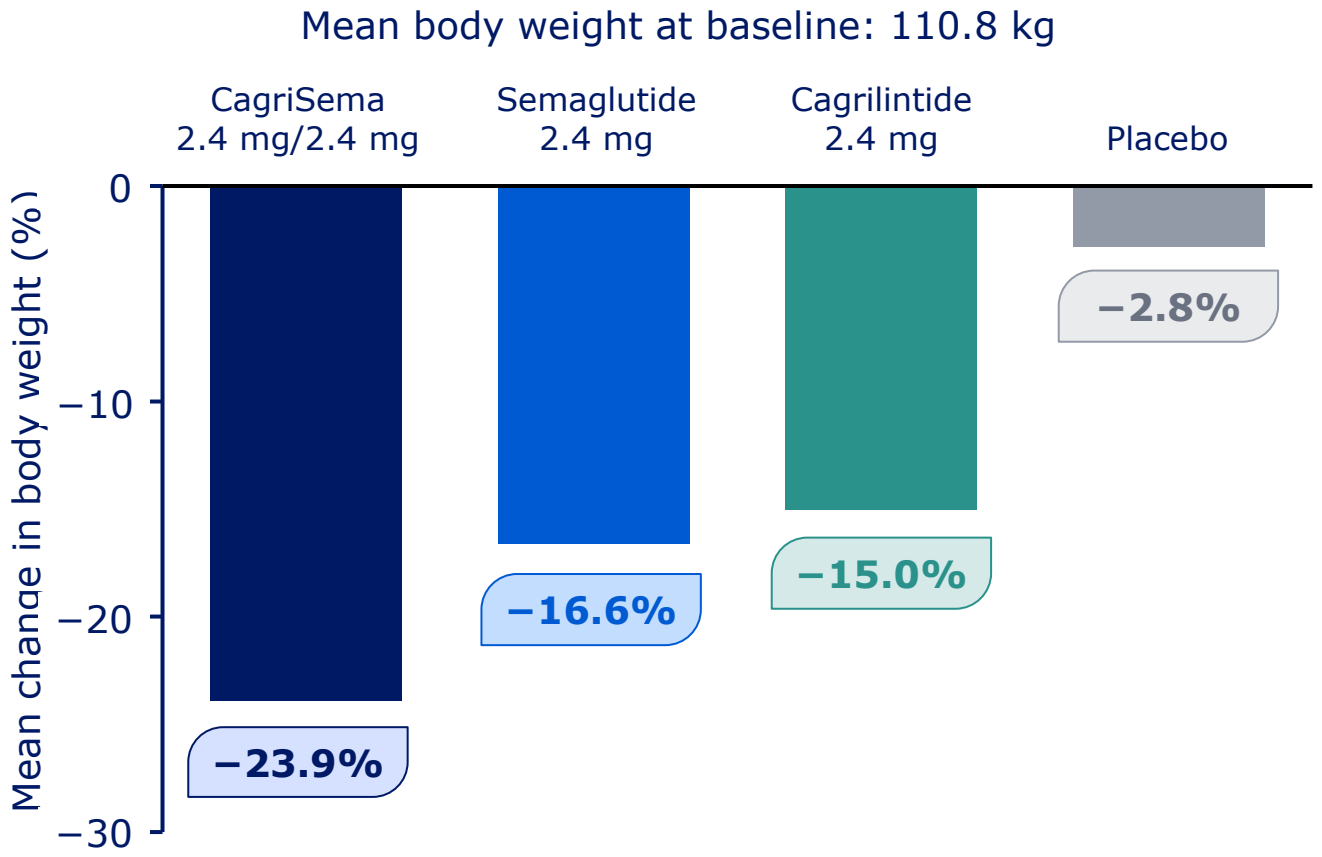
In the DXA subgroup, CagriSema 2.4 mg/2.4 mg demonstrated the greatest weight reduction at week 68



Data are for the trial product estimand: the difference in mean change in body weight from baseline to week 68 for all randomised participants, had all participants remained on randomised treatment (regardless of dose level) without initiation of rescue intervention, in which trial product is used as an adjunct to a reduced-calorie diet and increased physical activity. Body weight change via scale. DXA, dual-energy X-ray absorptiometry.

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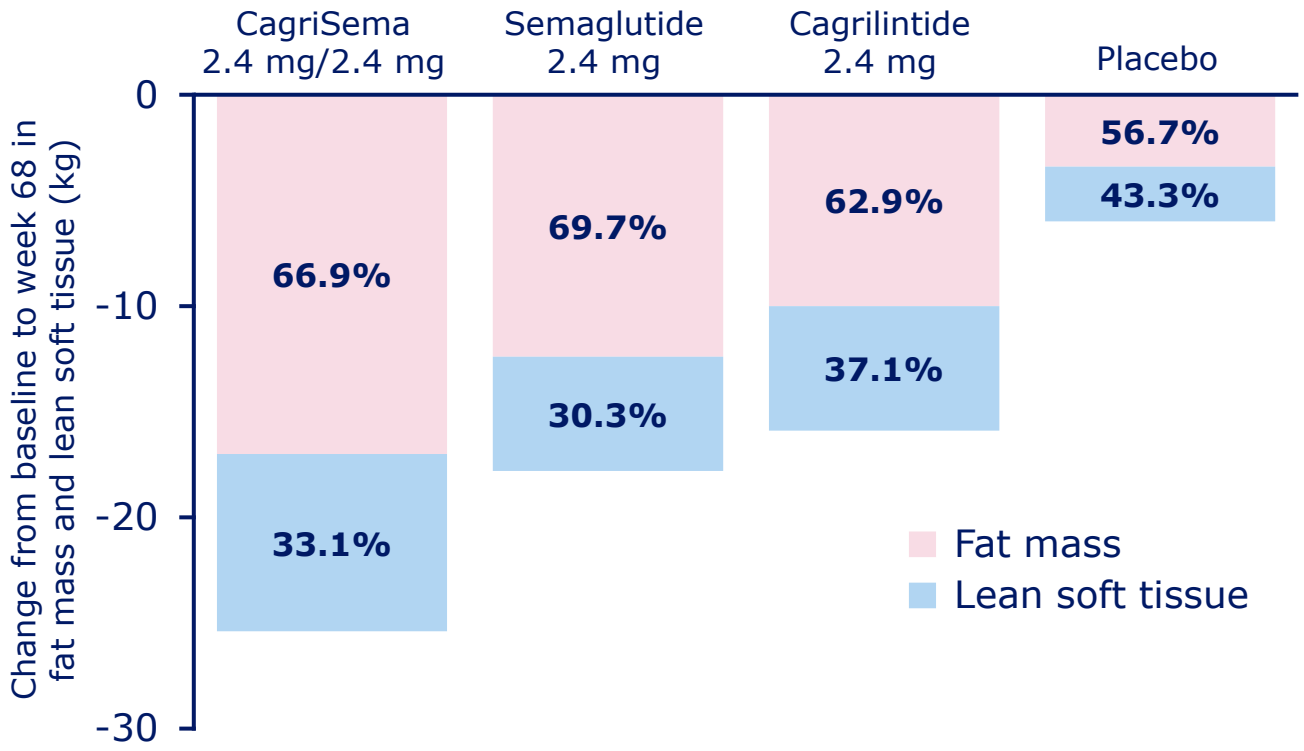
In the DXA subgroup, weight loss observed with CagriSema 2.4 mg/2.4 mg was primarily due to a loss of fat mass



Fat mass accounted for the majority of weight loss across all treatment arms

Estimated data according to the trial product estimand.
DXA, dual energy X-ray absorptiometry.

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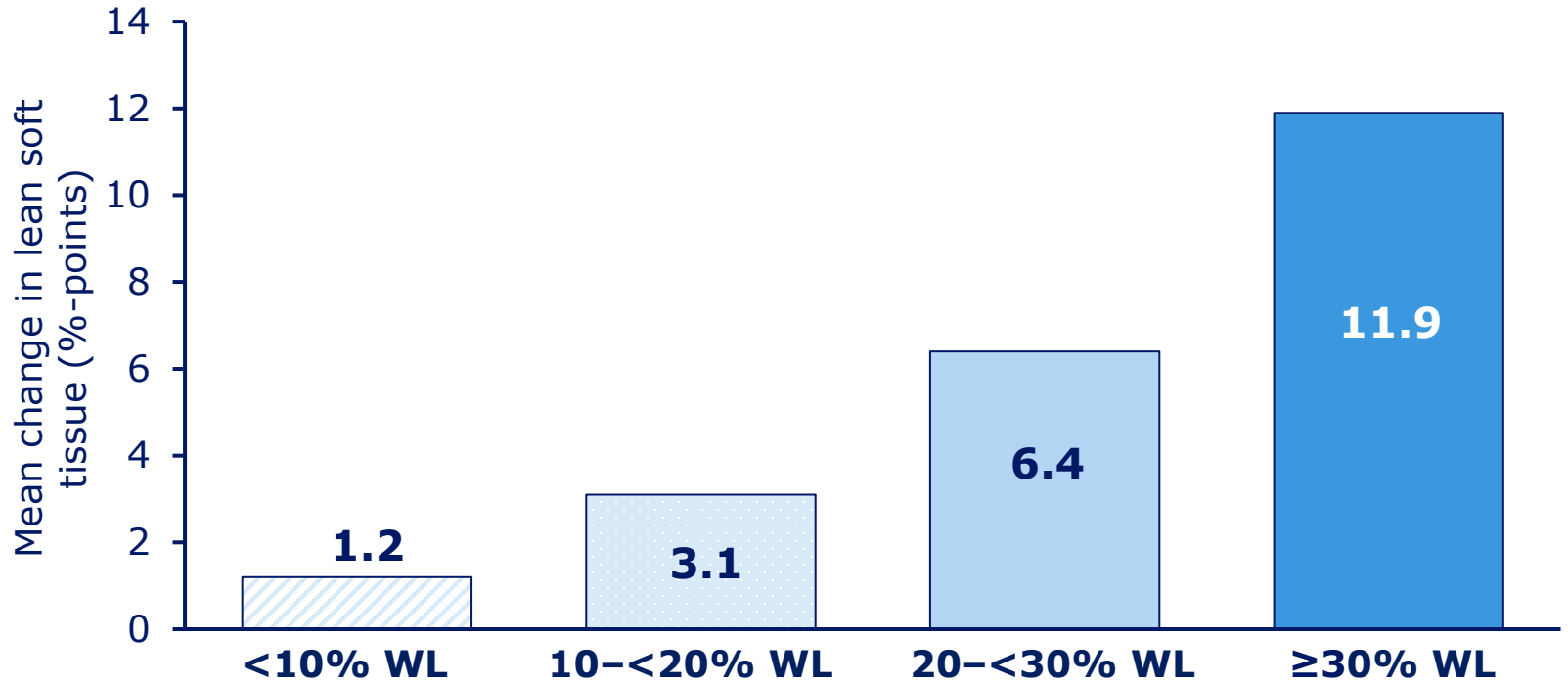
The proportion of lean soft tissue increased with weight loss in the CagriSema 2.4 mg/2.4 mg group



	<10% WL	10–<20% WL	20–<30% WL	≥30% WL
Baseline lean soft tissue (%):	57.0	56.3	53.1	51.3

In participants who lost ≥30% of body weight, the fat mass proportion decreased from 46.3% to 33.2%, whereas the lean soft tissue proportion increased from 51.3% to 63.2%

Change from baseline to week 68.
WL, weight loss.

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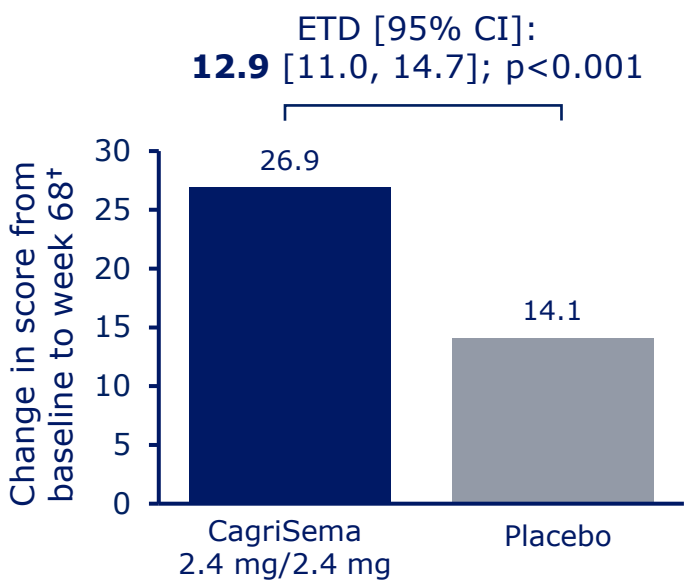
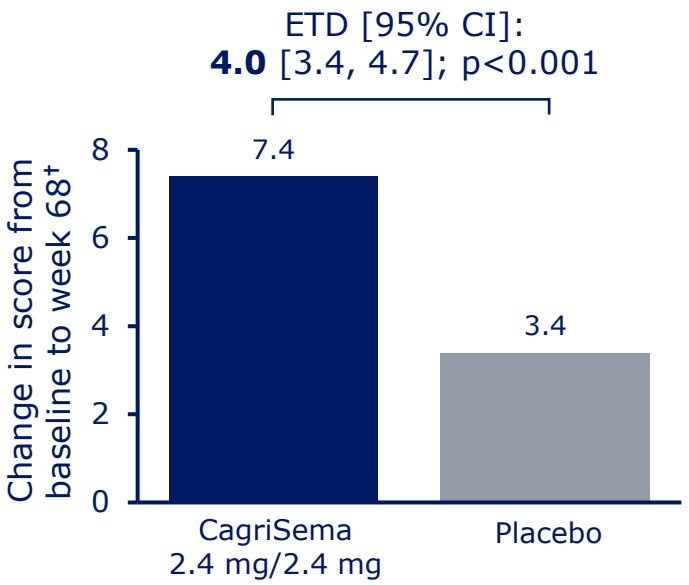
CagriSema 2.4 mg/2.4 mg led to significant improvements in physical function and no decrease in muscle strength

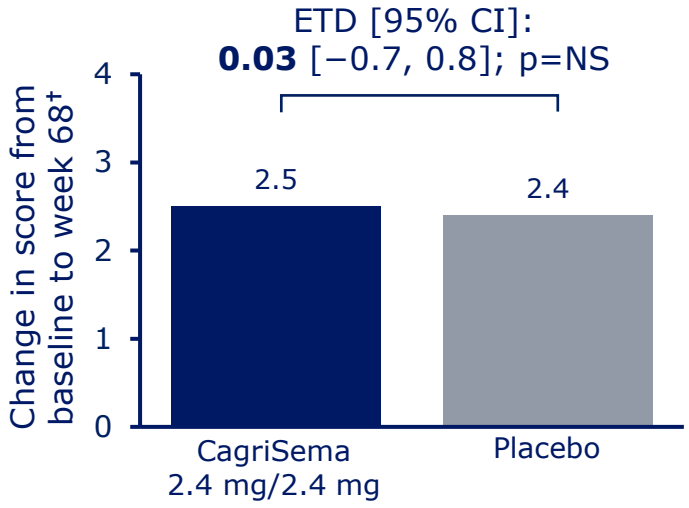
IWQoL-Lite-CT physical function



SF-36v2 physical functioning



Sit-to-stand test



CagriSema led to significant improvements in physical function versus placebo in both patient-reported outcome measures, IWQoL-Lite-CT and SF-36v2

†Estimated data according to the trial product estimand from the on-treatment period. Data are for treatment completers.
ETD, estimated treatment difference; CI, confidence interval; IWQoL-Lite-CT, Impact of Weight on Quality of Life-Lite Clinical Trials Version; NS, not significant; SF-36v2, SF-36v2 Health Survey acute version.

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Conclusions

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In the DXA subgroup of the REDEFINE 1 trial, weight loss observed with CagriSema 2.4 mg/2.4 mg was primarily due to a loss of fat mass (67%)

Despite CagriSema leading to an overall reduction in lean soft tissue, the proportion of lean soft tissue increased following weight loss, indicating an improvement in body composition

CagriSema-induced weight loss was not accompanied by a decrease in muscle strength, and led to an improvement in physical function, which was likely due to the associated improvement in body composition

DXA, dual energy X-ray absorptiometry.

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