STEP 3
WEIGHT MANAGEMENT WITH IBT

Wegovy® (semaglutide) injection versus Placebo

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STEP 3 was a **68-week**, Phase 3a, randomized, **placebo-controlled**, double-blind, multicenter trial in **611 adult patients** with obesity or overweight and at least 1 weight-related comorbidity.[1,a]

Select Eligibility Criteria[1]

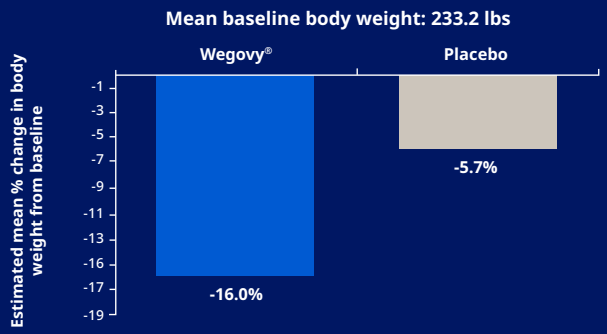
- Age ≥18 Years
- BMI: ≥30 kg/m² or ≥27 kg/m² with at least 1 weight-related comorbidity[a]
- A1C <6.5%
- Stable body weight for at least 90 days

Study Design[1]

Patients were randomized (**2:1**) to blinded treatment with **Wegovy®** or **placebo**, both of which were delivered in addition to **intensive behavioral therapy (IBT).**

Key Results at 68 Weeks[1]
Treatment policy estimand[b]

Coprimary efficacy endpoint: Mean % change in body weight from baseline to Week 68 with Wegovy® vs placebo



Analysis at Week 68	ETD	95% CI	*P*-value
Wegovy® vs placebo Coprimary endpoint	-10.3	[-12.0;-8.6]	<.001

Coprimary efficacy endpoint: Proportion of patients with a body weight reduction ≥5% at Week 68 vs placebo (observed values)

86.6% of patients on Wegovy®

47.6% of patients on placebo

Wegovy® vs placebo Coprimary endpoint	*P*-value
≥5%	<.001

Confirmatory secondary endpoints:

- **WEIGHT REDUCTION OF ≥10% AND ≥15%**
- **WAIST CIRCUMFERENCE**
- **SYSTOLIC BLOOD PRESSURE**
- **SF-36V2 PHYSICAL FUNCTIONING SCORE**

Safety[1]

- The most common adverse events (AEs) were gastrointestinal in nature, including nausea, vomiting, diarrhea, and constipation.
- More patients treated with Wegovy® discontinued treatment due to AEs than those treated with placebo (5.9% vs 2.9%, respectively), primarily due to gastrointestinal AEs (3.4% vs 0%, respectively).
- Serious AEs were reported in 9.1% of patients treated with Wegovy® and 2.9% of patients treated with placebo.

[a]Weight-related comorbidities include hypertension, dyslipidemia, obstructive sleep apnea and cardiovascular disease.
[b]The treatment policy estimand assessed effect regardless of rescue treatment or treatment discontinuation.
A1C: glycosylated hemoglobin; AE: adverse event; BMI: body mass index; CI: confidence interval; IBT: intensive behavioral therapy; lbs: pounds; SF-36V2: 36-Item Short-Form Health Survey, acute version.
Please note, if you are receiving this document by fax, it may contain icons and/or hyperlinks to websites/publications to expand on information. If you would like to receive this content via e-mail, please contact Novo Nordisk Medical Information at (800) 727-6500 or Scientific-Exchange.com.
Reference: 1. Wadden TA, Bailey TS, Billings LK, et al. Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial. *JAMA*. 2021;325(14):1405-1413

Medical Information Response

Wegovy® (semaglutide) injection vs. Placebo – Intensive Behavioral Therapy (STEP 3)

STEP 3

STEP 3 was a 68-week, Phase 3a, randomized, placebo-controlled, double-blind, multi-center trial in 611 U.S. patients.[1] Enrolled patients were ≥18 years of age, had a body mass index (BMI) of ≥30 kg/m^2 (obesity) or ≥27 kg/m^2 (overweight) with at least 1 weight-related comorbidity (e.g., hypertension, dyslipidemia, obstructive sleep apnea, or cardiovascular disease), had a glycosylated hemoglobin level of <6.5%, and had a stable body weight within 90 days prior to screening. As shown in **Figure 1**, patients were randomly assigned in a 2:1 ratio to receive treatment with once-weekly Wegovy® escalated to a maintenance dose of 2.4 mg or placebo, respectively. Patients received treatment as an adjunct to intensive behavioral therapy, which consisted of a low-calorie diet (1000-1200 kcal/day) provided as meal replacements during Week 0 to Week 8 followed by a hypocaloric diet (1200-1800 kcal/day) of conventional foods for the remainder of the trial, 100 minutes per week of moderate intensity physical activity that increased by 25 minutes every 4 weeks until 200 minutes per week was achieved, and 30 individual intensive behavioral therapy visits. Trial results analyzed the treatment differences from baseline to Week 68 using the treatment policy estimand where effects were assessed regardless of treatment discontinuation or rescue medication use. Please reference **Table 1** for key trial endpoints, while key safety data are summarized in **Table 2**.

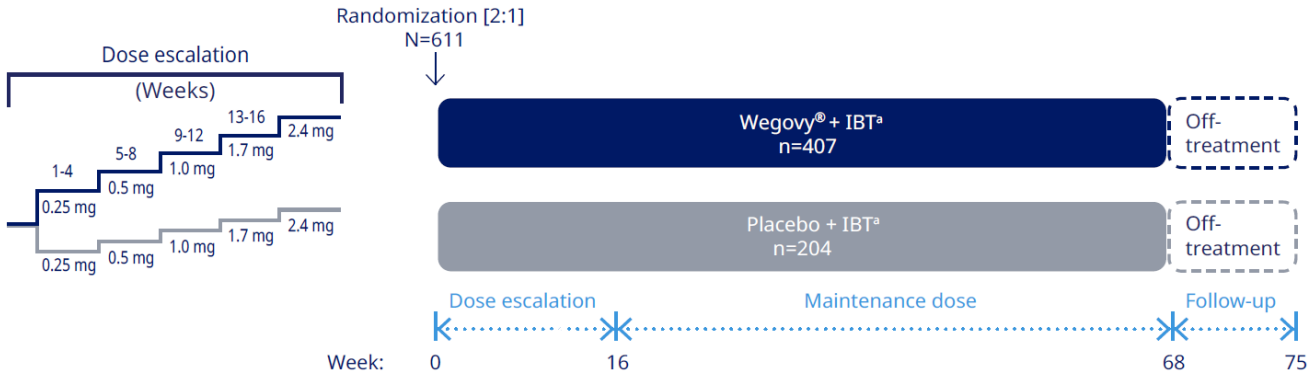


Figure 1. Trial design[1]

a. IBT consisted of an 8-week low calorie diet (1000-1200 kcal/day) followed by a hypocaloric diet (1200-1800 kcal/day) for the remainder of the trial, 100 minutes/week of physical activity that was increased by 25 minutes every 4 weeks to 200 minutes/week and 30 individual counseling sessions with a registered dietitian.

Abbreviations: IBT: intensive behavioral therapy

Table 1. Key Trial Endpoints in STEP 3[1]

	Wegovy® (n=407)	Placebo (n=204)
Baseline (Week 0) mean body weight — (lb)	235.7	228.6
COPRIMARY ENDPOINTS (BASELINE TO WEEK 68)		
Mean change in body weight — (%)	–16.0	–5.7
ETD (95% CI); *P*-value	–10.3 (–12.0 to –8.6); *P*<.001	
Patients with body weight reduction ≥5% — (%)	86.6	47.6
P-value	*P*<.001	
CONFIRMATORY SECONDARY ENDPOINTS (BASELINE TO WEEK 68)		
Patients with body weight reduction ≥10% — (%)	75.3	27.0
P-value	*P*<.001	
Patients with body weight reduction ≥15% — (%)	55.8	13.2
P-value	*P*<.001	
Baseline (Week 0) mean waist circumference — (in)	44.7	44.0
Mean change in waist circumference — (in)	–5.7	–2.5
ETD (95% CI); *P*-value	–3.3 (–4.0 to –2.6); *P*<.001	
Baseline (Week 0) mean systolic blood pressure — (mmHg)	124	124
Mean change in systolic blood pressure — (mmHg)	–5.6	–1.6
ETD (95% CI); *P*-value	–3.9 (–6.4 to –1.5); *P*=.001	
Baseline (Week 0) mean SF-36v2 physical functioning score[a]	51.9	52.1
Mean change in SF-36v2 physical functioning score	2.4	1.6
ETD (95% CI); *P*-value	0.8 (–0.2 to 1.9); *P*=.12	

a. Scores on the SF-36v2 are norm-based, transformed to a scale on which the 2009 general population of the United States has a mean score of 50 and a standard deviation of 10; higher scores indicate better quality of life.

Abbreviations: ETD: estimated treatment difference; CI: confidence interval; in: inches; SF-36v2: 36-Item Short-Form Health Survey, acute version

Table 2. STEP 3 Safety Overview[1,a]

Safety Outcomes, n (%)	Wegovy® (n=407)	Placebo (n=204)
Patients with ≥1 adverse event	390 (95.8)	196 (96.1)
Patients with ≥1 serious adverse event	37 (9.1)	6 (2.9)
Adverse events leading to treatment discontinuation	24 (5.9)	6 (2.9)
Gastrointestinal disorders	14 (3.4)	0
Adverse events reported in ≥10% of patients		
Nausea	237 (58.2)	45 (22.1)
Constipation	150 (36.9)	50 (24.5)
Diarrhea	147 (36.1)	45 (22.1)
Vomiting	111 (27.3)	22 (10.8)
Nasopharyngitis	90 (22.1)	49 (24.0)
Upper respiratory tract infection	85 (20.9)	44 (21.6)
Headache	78 (19.2)	20 (9.8)
Abdominal pain	54 (13.3)	10 (4.9)
Back pain	54 (13.3)	22 (10.8)
Dizziness	52 (12.8)	11 (5.4)
Fatigue	52 (12.8)	15 (7.4)
Flatulence	47 (11.5)	23 (11.3)
Gastroenteritis viral	42 (10.3)	13 (6.4)
Urinary tract infection	42 (10.3)	10 (4.9)
Abdominal distension	41 (10.1)	20 (9.8)
Sinusitis	39 (9.6)	26 (12.7)

a. Based on the safety analysis population, which includes all randomly allocated patients exposed to ≥1 dose of randomized intervention.

References

1. Wadden TA, Bailey TS, Billings LK, et al. Effect of Subcutaneous Semaglutide vs Placebo as an Adjunct to Intensive Behavioral Therapy on Body Weight in Adults With Overweight or Obesity: The STEP 3 Randomized Clinical Trial. *JAMA.* 2021;325(14):1403-1413. Link to Access the Full Text