Effect of semaglutide 2.4mg in adolescents with obesity
STEP TEENS Trial

STEP TEENS was a phase 3a, multinational, double-blind, parallel-group, randomized, placebo-controlled, 68-week clinical trial that evaluated the safety and efficacy of once-weekly subcutaneous semaglutide 2.4 mg in addition to lifestyle interventions for body weight management in adolescents (aged 12 to <18 years) with overweight or obesity with at least one weight-related comorbidity.[1]

Key Eligibility Criteria[1]

Adolescents (aged 12–<18 years) with BMI ≥95th percentile or ≥85th percentile with ≥1 weight-related comorbidity

- ≥1 unsuccessful dietary weight loss attempt
- For participants with T2D, HbA1c ≤10.0%
- Key exclusion criteria: >5 kg self-reported change in weight or AOM use ≤90 days of screening, Major depressive disorder ≤2 years of screening, or severe psychiatric disorders

Study Design[1]

Participants were randomized 2:1, stratified by sex and pubertal status, to once-weekly s.c. semaglutide 2.4 mg or placebo for 68 weeks with a 7-week follow-up.

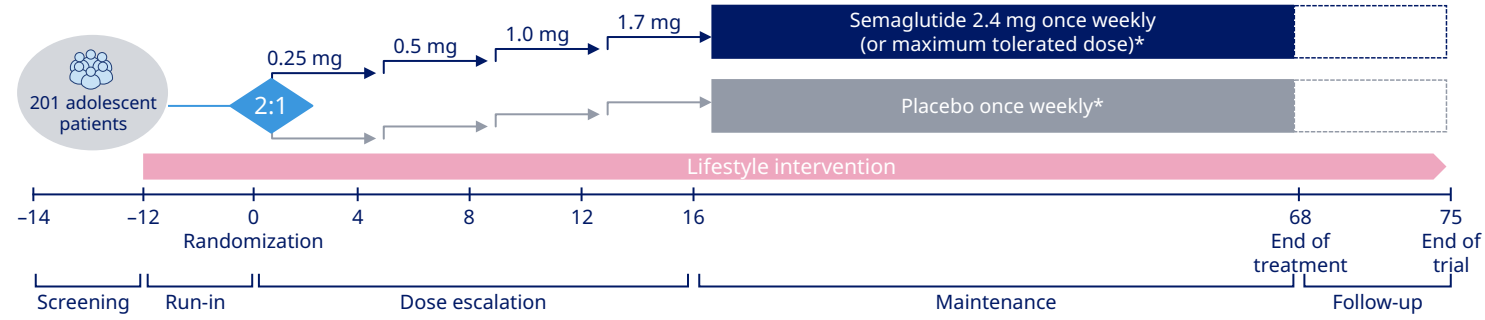


Figure 1 : STEP TEENS trial design

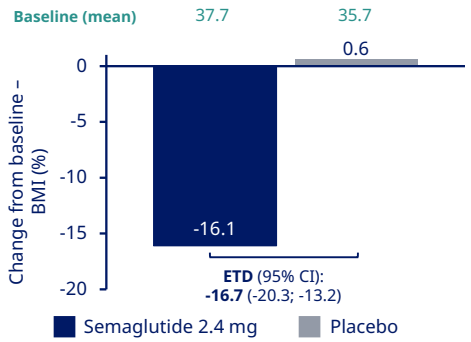
*As an adjunct to lifestyle intervention (–500 kcal/day diet with 150 minutes/week physical activity)

Key efficacy results[1]

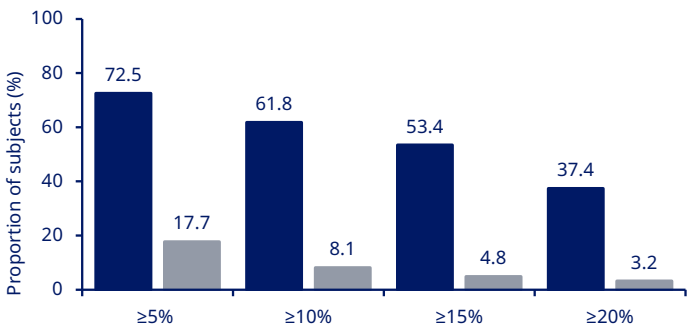
Table 1. End Points at Week 68 (Treatment Policy Estimand)*

End Point	Semaglutide (N = 134)	Placebo (N = 67)	Difference, Semaglutide vs. Placebo (95% CI)†	P Value
Primary end point				
Change in BMI — %	−16.1	0.6	−16.7 (−20.3 to −13.2)	<0.001
Secondary confirmatory end point				
≥5% reduction in body weight — no. of participants/ total no. (%)‡	95/131 (73)	11/62 (18)	14.0 (6.3 to 31.0)	<0.001

BMI change baseline to week 68



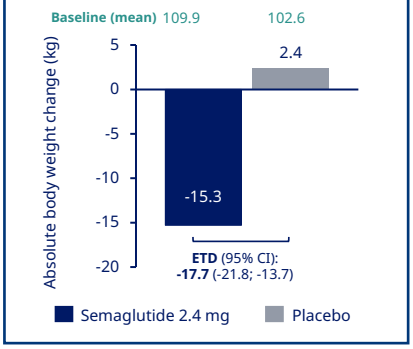
Weight loss ≥5%, ≥10%, ≥15% and ≥20% at week 68



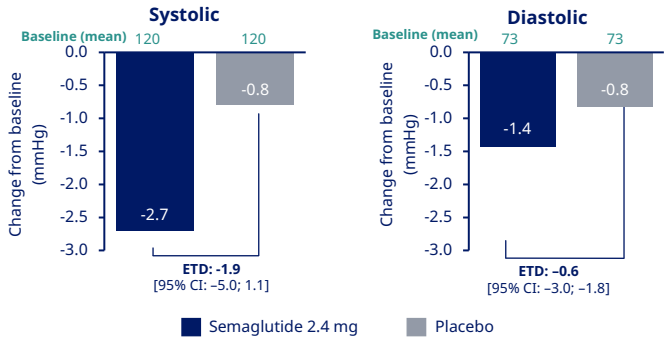
The analyses were performed on the basis of data from the in-trial observation period. † Data are the absolute differences between the estimated mean changes. The differences between mean percentage changes in BMI is expressed in percentage points. ‡ Data are the observed number of participants at week 68 for the in-trial period, and the difference is the estimated odds ratios.

Secondary supportive results[1]

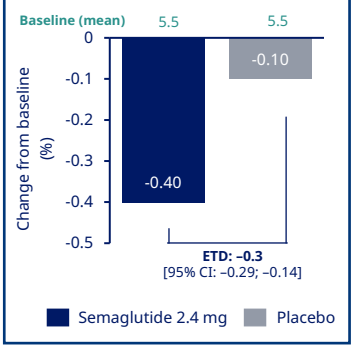
Body weight



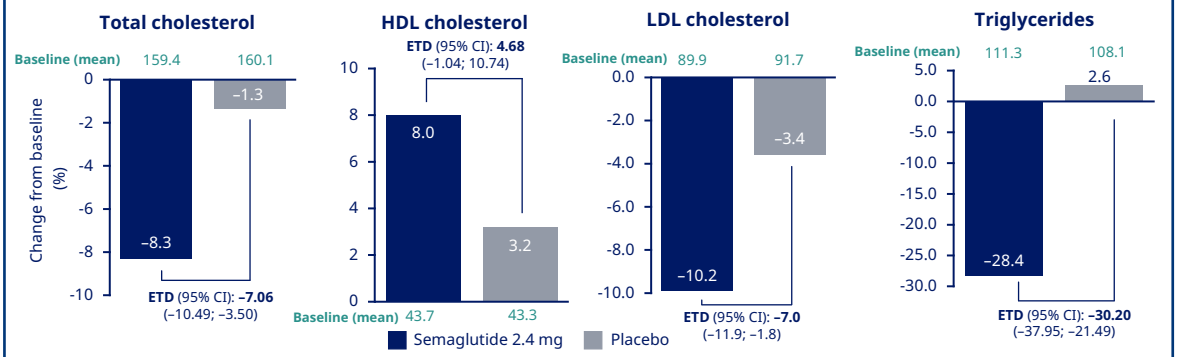
Blood pressure



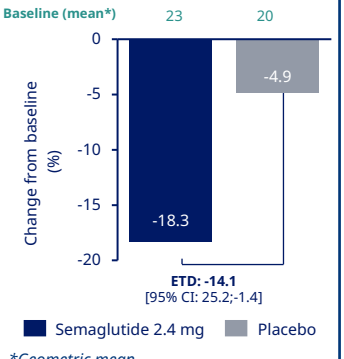
HbA_{1c}



Lipids



ALT



Safety[1]

- In total, 79% of semaglutide 2.4 mg treated patients compared to 82% of patients treated with placebo reported adverse events.
- AEs that led to permanent trial product discontinuation occurred in 5% and 4% of patients treated with semaglutide 2.4 mg and placebo, respectively.
- The most frequently reported AEs were GI disorders, primarily nausea, vomiting and diarrhea.
- Acute gallbladder disease was reported in 5 patients (4%) treated with semaglutide 2.4 mg, all of whom had cholelithiasis and 1 patient with concurrent cholecystitis. No patients treated with placebo reported cholelithiasis.
- No cases or instances of pancreatitis, acute renal failure, diabetic retinopathy or severe hypoglycemia were reported.
- Fewer patients in the semaglutide 2.4 mg arm versus the placebo arm reported psychiatric AEs (7% vs 15%, respectively).

Table 2. Adverse Events*

Event	Semaglutide 2.4 mg (N = 133)	Placebo (N = 67)
	no. of participants (%)	no. of participants (%)
Any adverse event	105 (79)	55 (82)
Serious adverse events	15 (11)	6 (9)
Adverse events leading to discontinuation of trial regimen	6 (5)	3 (4)
• Gastrointestinal disorders	3 (2)	1 (1)
Fatal adverse events†	0	0
Selected Gastrointestinal adverse events‡		
Nausea	56 (42)	12 (18)
Vomiting	48 (36)	7 (10)
Diarrhea	29 (22)	13 (19)
Abdominal pain	20 (15)	4 (6)
Abdominal pain upper	11 (8)	9 (3)
Gastroenteritis	9 (7)	2 (3)
Constipation	8 (6)	1 (2)

** Safety was assessed in all participants who underwent randomization and were exposed to at least one dose of semaglutide or placebo. Shown are the observed data in the safety analysis population during the on-treatment period, unless otherwise indicated. † Data are the observed data in the safety population from the in-trial period (the time from randomization to the last contact with a trial site, regardless of discontinuation of semaglutide or placebo or the use of rescue interventions). ‡ Adverse events are listed according to the preferred term in the Medical Dictionary for Regulatory Activities (MedDRA), version 24.1.*

Abbreviations: *A1C, glycated hemoglobin; ALT, alanine transaminase; BMI: body mass index; CI, confidence interval; Covid-19 denotes coronavirus disease 2019, ETD, estimated treatment difference; GI, gastrointestinal; HDL, high-density lipoprotein; HF, heart failure; HR, hazard ratio; LDL, low-density lipoprotein; N, number of patients*

Reference: 1. Weghuber et al. N Engl J Med 2022;387:2245–2257