

Semaglutide for weight loss

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Clinical question

Is semaglutide (SGT) effective for weight loss?

Bottom line

Used with lifestyle changes, 2.4 mg of subcutaneous SGT weekly resulted in a mean 10% to 15% weight loss (10 to 15 kg) over 68 weeks versus 2% to 3% (3 to 4 kg) with placebo (PC). Most (70% to 80%) lost 5% or more of their body weight. About 75% had gastrointestinal side effects, but few discontinued treatment. Weight was regained on medication discontinuation.

Evidence

Differences were statistically significant unless noted.

- In 4 RCTs, patients (baseline weight 96 to 105 kg) were treated for weight loss with 2.4 mg of subcutaneous SGT weekly and lifestyle interventions (counseling, diet, and physical activity).¹⁻⁴
 - An RCT of nondiabetic patients (N=1961)¹: After 68 weeks, mean weight loss was 15% (15 kg) versus 2% (3 kg) PC. The proportion of those who lost weight ($\geq 5\%$) was 86% versus 32% (PC), with a number needed to treat (NNT)=2, while the proportion who lost more weight ($\geq 10\%$) was 69% versus 12% (PC), NNT=2. Weight loss plateaued around week 60.
 - Gastrointestinal adverse effects (AEs): 74% versus 48% (PC), number needed to harm (NNH)=3. Withdrawals due to AEs were 7% versus 3% (PC), NNH=25.
 - Similar results in an RCT (N=611) of SGT with intensive lifestyle interventions: 16% (17 kg) versus 6% (6 kg) PC.²
 - Dose-finding RCT³ of diabetic patients (N=1210) given either 2.4 mg of SGT weekly, 1.0 mg of SGT weekly, or PC: After 68 weeks, mean weight loss was 10% (2.4 mg), 7% (1.0 mg), and 3% (PC). Proportion who lost weight ($\geq 5\%$) was 69% (2.4 mg) versus 57% (1.0 mg) versus 29% (PC). For 2.4 mg versus 1.0 mg, NNT=9.
 - The AEs were similar between doses.
 - Weight-maintenance RCT (N=803)⁴: Nondiabetic participants were given 2.4 mg of SGT weekly for 20 weeks and then randomized to either continued SGT or PC. After 48 weeks, the continued SGT group lost 8% body weight compared with a 7% weight gain in the PC group.

Context

- Weight loss with oral SGT studied as a secondary outcome in cardiovascular disease and glucose-lowering

trials found that weight loss was 4.6% (4.2 kg) versus 0.9% (0.8 kg) with PC at 15.9 months.⁵

- In an SGT-sponsored RCT, high-dose SGT (0.4 mg/day) was superior to liraglutide (3 mg/day). Weight loss was 14% (17 kg) SGT versus 8% (8 kg) liraglutide. Weight loss was similar between 0.1 mg of SGT daily and liraglutide.⁶
- Semaglutide (2.4 mg) is not available now in Canada, but lower doses are⁷ (1 mg/week costs about \$200/month⁸).

Implementation

Besides weight loss, SGT increased quality of life for 40% to 50% of participants compared with about 30% taking PC.¹ Semaglutide is usually started at 0.25 mg weekly and is increased by 0.25 mg every 4 weeks until the target dose is reached (as tolerated).⁹ Nausea and gastrointestinal upset are reported AEs, particularly during dose escalation.^{1,9} Adherence to weekly subcutaneous injections may be better than for daily injections.¹⁰ Other glucagon-like peptide 1 agonists and SGT should likely be avoided in patients with history of medullary thyroid carcinoma, pancreatitis, or tachyarrhythmias.⁹

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Competing interests
None declared

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the College of Family Physicians of Canada.

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