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PUBLISHED NOVEMBER 15, 2021

Higher Semaglutide Doses Even Better for Weight Loss and Diabetes Control?

By staff

The recent **SUSTAIN FORTE study**, published in September 2021 in *Lancet Diabetes & Endocrinology*, reports that higher doses of the glucagon-like peptide 1 (GLP-1) agonist semaglutide could offer another treatment option and appear to result in even better outcomes for both weight loss and diabetes. This dosing alternative is currently under FDA review, but the authors are hopeful given the results they obtained using the higher dose.

Dr. Juan P. Frías, a clinical researcher at the National Research Institute, Los Angeles, California, and colleagues set out to further explore the extent to which higher doses of semaglutide could improve diabetic control and weight loss. Findings from the original SUSTAIN trial were limited to only 0.5-mg and 1-mg doses of semaglutide. In the previous trial, despite superior blood glucose control compared with other GLP-1 receptor agonists, fewer than one-half of subjects reached the target HbA1C, which was set at less than 7% with the 1-mg dose. The authors noted that dose-dependent reductions in both body weight and HbA1C were seen at higher doses, which did not appear to be associated with any newly emergent or exacerbated preexisting safety concerns.

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The researchers conducted a 40-week, randomized, double-blind, phase IIIB trial (SUSTAIN FORTE) at 125 outpatient clinics in 10 countries. The subjects were adults aged 18 years and older who were determined to have suboptimally controlled type 2 diabetes with HbA1C of 8.0% to 10.0% and were treated with metformin with or without sulfonylurea; they were randomly assigned to receive either a 1-mg (n = 481) or 2-mg (n = 480) once-weekly semaglutide dose. For each group, average duration of diabetes was roughly 10 years (baseline HbA1C of 8.8%) and 9 years (baseline HbA1C of 8.9%), and BMI was 34.4 and 34.8, respectively. Participants, site personnel, the clinical study group, and investigators were blinded to the assigned treatment.

The research outcomes were reported after 40 weeks, with subjects taking the 1-mg dose experiencing a 1.9% decrease in HbA1C compared with 2.2% in those taking the 2-mg dose. In terms of weight loss, 28% of participants on semaglutide 2 mg experienced a weight loss of at least 10% compared with 23% of those on semaglutide 1 mg, and 59% of participants experienced at least 5% weight loss on semaglutide 2 mg compared with 51% of participants on the 1-mg dose.

The authors concluded that despite GLP-1 agonists being an established treatment option via their inhibition of glucagon release and promotion of insulin secretion, differences exist in different available agents regarding their potential to improve glucose control, weight loss, and other cardiovascular risks.

They further reported that their study results demonstrate that this specific once-weekly higher-dose semaglutide (2 mg) is "more efficacious than 1 mg, with similar safety profile, for people with type 2 diabetes. The 2-mg dose should provide a simple intensification option for patients given semaglutide in need of additional glycemic control via escalating their existing treatment."

The authors acknowledged that their study was funded by Novo Nordisk, the manufacturers of the brand-name drug Wegovy.

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