Effects of once-weekly semaglutide vs. canagliflozin on body composition in type 2 diabetes: a substudy of the SUSTAIN 8 trial

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Background and aims: SUSTAIN 8 was a randomised, double-blind, double-dummy, phase 3 trial of semaglutide 1.0 mg once weekly vs. canagliflozin 300 mg once daily over 52 weeks in adults with type 2 diabetes (T2D) on stable treatment with metformin. In SUSTAIN 8, treatment with semaglutide led to superior reductions in HbA$_{1c}$ and body weight vs. daily canagliflozin. Because these two agents have different mechanisms for weight loss, whole-body dual-energy X-ray absorptiometry (DXA) was performed in a subset of subjects to investigate the effects of semaglutide vs. canagliflozin on body composition.

Materials and methods: A total of 178 subjects underwent DXA to assess change in total fat mass. Prespecified supportive secondary measures of body composition included changes in total lean mass, ratio of total fat mass to total lean mass and visceral fat mass. Additional parameters such as waist circumference were also assessed *post hoc*. Data from the on-treatment without rescue medication period were analysed using ANCOVA with treatment, region and baseline values as fixed effects using multiple imputation for missing data where missing values were imputed using observed data from subjects in the same treatment group.

Results: In this subset of the SUSTAIN 8 population (n=178/788), the overall reduction in total fat plus lean mass was 5.7 kg with once-weekly semaglutide vs. 4.1 with canagliflozin once daily (**Table**). Total fat mass decreased by 3.4 and 2.6 kg in the semaglutide and canagliflozin groups, respectively (estimated treatment difference [ETD] –0.79 kg [95% confidence interval (CI): –2.10;0.51]). Similarly, total lean mass decreased by 2.3 and 1.5 kg (ETD –0.78 kg [95% CI: –1.61;0.04]). These changes resulted in slight decreases in the ratio of total fat mass to total lean mass in both groups; similar reductions were observed for visceral fat mass in both treatment arms (**Table**).

Conclusion: Both once-weekly semaglutide 1.0 mg and canagliflozin 300 mg once daily showed beneficial effects on body composition, including reduction in total and visceral fat mass, after 52 weeks treatment in subjects with T2D. There was no statistically significant difference between the arms for any of the body composition endpoints.

Table. SUSTAIN 8 substudy: key baseline characteristics and changes in body composition from baseline at week 52.

	Semaglutide 1.0 mg OW (n=88)	Canagliflozin 300 mg OD (n=90)	Analysis ETD [95% CI]
Baseline characteristics			
Age, years	57.8 (9.9)	58.6 (10.1)	
Diabetes duration, years	8.8 (5.8)	8.5 (5.2)	
Body weight, kg	89.0 (18.2)	87.6 (18.2)	
Changes in body composition at 52 weeks			
Total fat mass			
Baseline, kg / %	33.9 (11.9) / 38.0 (8.4)	32.5 (10.0) / 37.3 (7.3)	
Change at week 52, kg / %-point	–3.4 (0.51) / –1.43 (0.39)	–2.62 (0.45) / –1.21 (0.35)	–0.79 [–2.10;0.51] / –0.21 [–1.26;0.84]
Total lean mass			
Baseline, kg / %	51.3 (10.1) / 59.1 (8.0)	51.3 (10.7) / 59.7 (6.9)	
Change at week 52, kg / %-point	–2.26 (0.31) / –1.24 (0.39)	–1.48 (0.28) / –1.10 (0.34)	–0.78 [–1.61;0.04] / 0.14 [–0.89;1.18]
Total fat plus lean mass, kg			
Baseline	85.2	83.9	
Change at week 52	–5.7	–4.1	
Total fat mass / total lean mass ratio, kg			
Baseline	0.7 (0.23)	0.7 (0.20)	
Change at week 52	–0.04 (0.01)	–0.03 (0.01)	–0.01 [–0.04;0.02]
Visceral fat mass			
Baseline, kg / %	1.5 (0.8) / 43.7 (16.2)	1.5 (0.8) / 44.0 (15.3)	
Change at week 52, kg / %-point	–0.18 (0.05) / –0.94 (0.94)	–0.11 (0.04) / 0.44 (0.69)	–0.07 [–0.20;0.06] / –1.38 [–3.65;–0.88]
Waist circumference, cm			
Baseline	104.0 (13.5)	105.9 (13.1)	
Change at week 52*	–3.9 (5.6)	–2.5 (5.5)	

*Not prespecified for the substudy. Data for changes at week 52 are mean (standard error). All other data are mean (standard deviation) unless otherwise specified. CI, confidence interval; ETD, estimated treatment difference; OD, once daily; OW, once weekly.