Impact of Semaglutide on Body Composition in Adults with Overweight or Obesity: Exploratory Analysis of the STEP 1 Study

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Background: Central obesity is associated with increased risk of cardiometabolic disease. Weight loss reduces lean muscle mass, potentially impacting resting energy expenditure and/or physical functioning. This analysis of the STEP 1 trial evaluated the impact of subcutaneous (s.c.) semaglutide, a glucagon-like peptide-1 analogue, on body composition in adults with overweight/obesity using dual energy X-ray absorptiometry (DEXA).

Methods: In STEP 1, 1961 adults aged ≥18 years with body mass index (BMI) ≥27 kg/m2 with ≥1 weight-related comorbidity or BMI ≥30 kg/m2, without diabetes, were randomized to s.c. semaglutide 2.4 mg once-weekly or matched placebo (2:1) for 68 weeks, plus lifestyle intervention. Participants with BMI ≤40 kg/m2 from 9 sites were eligible for the substudy. Total fat mass, total lean body mass and regional visceral fat mass were measured using DEXA at screening and week 68; visceral fat mass was calculated in the L4 region (both males/females), android region (males), or gynoid region (females), depending on site scanner methodology. Proportions of total fat and lean body mass are shown relative to total body mass; proportion of visceral fat mass is expressed relative to region assessed.

Results: This analysis included 140 participants (semaglutide n=95; placebo n=45) (mean weight 98.4 kg, BMI 34.8 kg/m2; 76% female). Baseline body composition was similar in those receiving semaglutide and placebo (total fat mass proportion: 43.4% vs 44.6%; regional visceral fat mass proportion: 33.8% vs 36.3%; total lean body mass proportion: 53.9% vs 52.7%; respectively). Percentage change in body weight from baseline to week 68 was -15.0% with semaglutide vs -3.6% with placebo. This resulted in reductions from baseline with semaglutide in total fat mass (-19.3%) and regional visceral fat mass (-27.4%), leading to 3.5%-point and 2.0%-point reductions in the proportions of total fat mass and visceral fat mass, respectively. Total lean body mass decreased from baseline (-9.7%); however, the proportion relative to total body mass increased by 3.0%-points. An increasing improvement in lean body mass:fat mass ratio was seen with semaglutide with increasing weight loss from baseline to week 68 (continuous

data). Overall, the ratio increased from baseline (1.34 [95% CI: 1.22, 1.47]) to week 68 by 0.23 [0.14, 0.32], with greater improvement in those with ≥15% weight loss (n=44; 0.41 [0.28, 0.53]) vs <15% weight loss (n=39; 0.03 [-0.05, 0.12]) (observed, dichotomized data; no imputation for missing data). There were no major changes in body composition with placebo from baseline to week 68.

Conclusion: In adults with overweight/obesity, semaglutide 2.4 mg was associated with reduced total fat mass and regional visceral fat mass, and an increased proportion of lean body mass. Greater weight loss was associated with greater improvement in body composition (lean body mass:fat mass ratio).