Efficacy and Safety of Semaglutide 7.2 mg in Obesity —STEP UP Trial

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**Introduction and Objective:** To assess efficacy and safety of semaglutide (sema) 7.2 mg in adults with obesity. #

**Methods:** This multicenter, double-blind trial (NCT05646706) included adults with BMI ≥30 kg/m2 without T2D, randomized 5:1:1 to once-weekly s.c. sema 7.2 mg, 2.4 mg or placebo (pbo) plus lifestyle intervention, for 72 weeks with 9-week off-treatment follow-up. Co-primary endpoints were relative weight loss (%WL) and proportion reaching ≥5% WL with sema 7.2 mg vs pbo from baseline to week 72. Confirmatory endpoints were %WL with 7.2 mg vs 2.4 mg, waist circumference (WC) change (cm) and proportion reaching ≥10% to ≥25% weight loss thresholds vs pbo and ≥20% and ≥25% vs 2.4 mg. Safety was assessed.

**Results:** In total (7.2 mg, n=1005; 2.4 mg, n=201; pbo, n=201), 74% were female, mean age was 47 yrs, weight 113 kg, BMI 39.9 kg/m2 and WC 119 cm. Most treatment completers reached the max dose (7.2 mg, 75.4%; 2.4 mg, 89.3%; pbo, 96.5%). Mean %WL was greater with sema 7.2 mg (18.7%) vs 2.4 mg (15.6%) or pbo (3.9%) (p<0.001), with significant differences in attainment of %WL thresholds (Fig.). WC was reduced with sema 7.2 mg vs pbo (p<0.001). Gastrointestinal adverse events (AEs) reported by 70.8%, 61.2% and 42.8% of participants with sema 7.2 mg, 2.4 mg and pbo, respectively; 3.3%, 2.0% and 0% discontinued due to these AEs. Serious AEs reported by 6.8%, 10.9% and 5.5% of participants, respectively.

**Conclusion:** Sema 7.2 mg was superior to 2.4 mg and pbo for %WL in adults with obesity, with a similar safety profile to sema 2.4 mg.