Presentation 1012-P / 1012 The Effects of Semaglutide on ß-cell Function in Subjects with Type 2 Diabetes

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Abstract:
Subjects with type 2 diabetes (T2D, n=75; mean HbA_{1c} 7.3%, duration of T2D 8.5 years, BMI 29.6 kg/m^2, age 56 years, 68% male) were randomized 1:1 to receive semaglutide, a once-weekly GLP-1 analog (escalated to 1.0 mg) or placebo for 12 weeks. Untreated healthy subjects (n=12; mean BMI 26.8 kg/m^2, age 43 years, 67% male) were included in a graded glucose infusion (GGI) test. The semaglutide:placebo ratio for change from baseline to end-of-treatment AUC following intravenous glucose tolerance (Figure 1), arginine stimulation and GGI tests (Figure 2) showed larger insulin response for semaglutide ($p<0.0001$). After 12 weeks, the insulin secretion rate during GGI tests showed that β-cell responsiveness in semaglutide-treated subjects with T2D was comparable to that of untreated healthy controls (Figure 2). There were no safety or tolerability issues.

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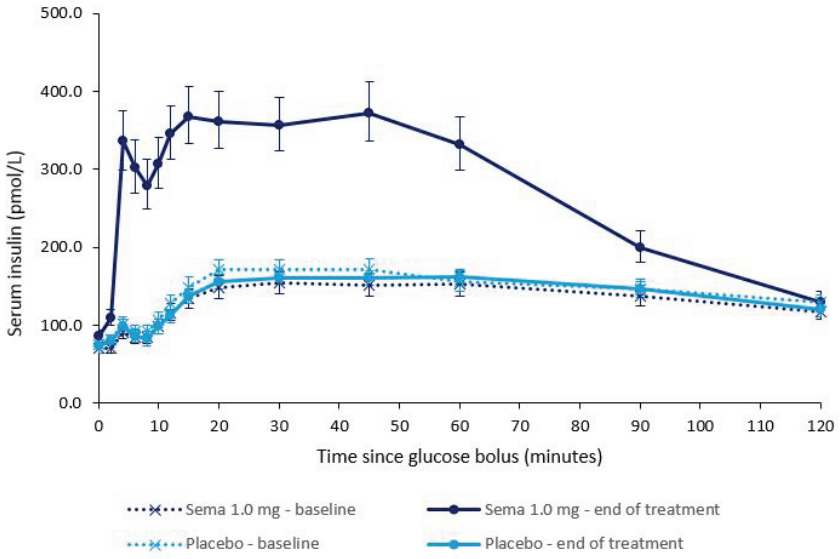
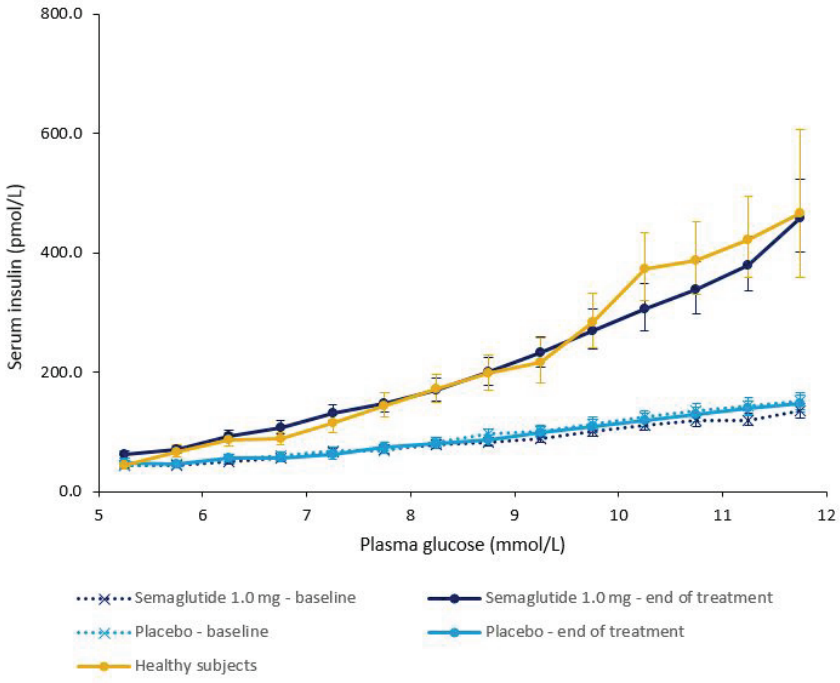
Figure 1. Insulin response to the intravenous glucose tolerance test in subjects with T2D receiving semaglutide or placebo.



After intravenous infusion with a 25 g glucose bolus, the semaglutide:placebo ratio for change from baseline to end-of-treatment in the Area Under the Curve (AUC) was larger for first-phase (0–10 min) and second-phase (10–120 min) insulin response (estimated treatment ratio: 3.02 and 2.10, respectively; p<0.0001 for both).

Figure 2. Insulin response to a graded glucose infusion in subjects with T2D and healthy controls.



A continuous glucose infusion was adjusted to achieve target levels of 5, 6, 7, 8, 9, 10, 11 and 12 mmol/L over 180 min, with blood drawn for analysis throughout. Both the insulin secretion rate and slope at end of treatment for semaglutide were comparable to those of untreated healthy subjects.