**EXENATIDE ACHIEVED EQUIVALENT GLYCEMIC CONTROL TO INSULIN GLARGINE WITH WEIGHT REDUCTION, INDEPENDENTLY FROM BASELINE BMI, IN METFORMIN AND SULFONYLUREA-TREATED TYPE-2 DIABETES**

Heine Robert J.\(^1\); Van Gaal Luc F.\(^2\); Johns Don\(^3\); Mihm Michael J.\(^3\); Gentilella Raffaella\(^4\); Widel Mario H.\(^3\); Brodows Robert G.\(^3\)

1 Diabetes Center, Department of Endocrinology, VU University Medical Center, Amsterdam, The Netherlands; 2 Department of Diabetology, Metabolism and Clinical Nutrition, Faculty of Medicine, University Hospital Antwerp, Belgium; 3Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN, USA; 4Eli Lilly Italy, Florence, Italy

**Background:** Clinical studies have shown that exenatide improves glycaemic control, and is associated with weight reduction, reduced postprandial glucose excursions, and a low incidence of hypoglycaemia in type 2 diabetes (NIDDM) patients (pts) inadequately controlled by MET, SFU and/or a TZD. The addition of basal insulin is currently common practice when oral medications fail, but can be associated with increased hypoglycaemia, inadequate postprandial glucose control, and weight gain. The primary aim of this trial was to determine whether exenatide (E) can be used as an alternative to basal insulin (insulin glargine, G) NIDDM patients sub-optimally controlled with MET + SFU. Additional analyses include the differential effects of the treatments on body weight and glycemic control on the basis of baseline (BL) BMI.

**Methods:** 82 outpatient study centers in 13 countries participated in this 26-week trial. NIDDM pts (HbA\(_1c\) 7.0-10.0%) were randomized to E (5 µg BID for first 4 wks, 10 µg BID remainder of study, n=283) or G (QD titrated to FBG<5.6 mM, n=268), adjunctive to pre-existing MET + SFU. The primary endpoint was the change in HbA\(_1c\) from BL to Week 26. Body weight change was evaluated as a secondary endpoint and was analyzed by BL BMI in a 2-way ANOVA post-hoc analysis.

**Results:** In the overall treatment groups, E and G resulted in similar reductions in HbA\(_1c\) (E -1.1±0.1%, G -1.1±0.1%), and proportion of pts to target HbA\(_1c\) ≤7% at endpoint (E: 46%, G: 48%). Body weight changes at endpoint were -2.3±0.2 kg for E vs +1.8±0.2 kg for G (p<0.0001). Pts with poor BL glycemic control (HbA\(_1c\) ≥7.5%) were subdivided by BL BMI, and groups with BL values of ≥25 to <30 Kg/m\(^2\) (E: n=85; G: n=76) and ≥30 and <35 Kg/m\(^2\) (E: n=75; G: n=84) were investigated. For BL BMI ≥25 to <30 Kg/m\(^2\), the mean HbA1c reduction was 1.0% in E-treated subjects and 1.1% in G-treated pts (p<0.0001 vs BL HbA\(_1c\) for both groups, NS between treatments); for BL BMI ≥30 and <35 Kg/m\(^2\), 1.3% and 1.1% HbA\(_1c\) reduction was observed in E- and G-treated pts, respectively (p<0.0001 vs BL HbA\(_1c\) for both groups, NS between treatments). A mean reduction of ~1.9 kg was observed in E-treated pts with BL BMI ≥25 to ≤30 Kg/m\(^2\) versus +1.7 kg gain for G-treated subjects (p<0.0001 vs BL HbA\(_1c\) for both treatments); for BL BMI ≥50 and ≤35 Kg/m\(^2\), 1.3% and 1.1% HbA\(_1c\) reduction was observed in E- and G-treated pts, respectively (p<0.0001 vs BL HbA\(_1c\) for both groups, NS between treatments). A mean reduction of ~1.9 kg was observed in E-treated pts with BL BMI ≥25 to ≤30 Kg/m\(^2\) versus +1.7 kg gain for G-treated subjects (p<0.0001 vs BL for both treatments; p<0.0001 for E vs G); a ~1.3 kg decrease was observed for E-treated pts ≥30 and ≤35Kg/m\(^2\) vs a weight gain of +2.3 kg in G-treated pts (p<0.0045 and <0.0001 vs BL, respectively; p<0.0001 for E vs G).

**Conclusion:** Fixed dose E achieved similar improvements in overall glycaemic control to G titration in pts with long-standing NIDDM inadequately controlled by MET + SFU. E was additionally associated with progressive weight reduction, in the overall patient sample, as well as in subdivisions based on BL BMI.