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

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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 type2 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 13countries participated in this 26week trial. NIDDM pts(HbA_{1c} 7.0-10.0%)were randomized to E(5µg BID for first 4wks,10µg BID remainder of study, n=283)or G QD(titrated to FBG<5.6mM,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 $HbA_{1c}\leq 7\%$ at endpoint(E: 46%,G: 48%).Body weight changes at endpoint were -2.3±0.2kg for E vs +1.8±0.2kg for G($p<0.0001$).Pts with poor BL glycemic control($HbA_{1c}\geq 7.5\%$)were subdivided by BL BMI, and groups with BL values of $\geq$25 to $\leq 30 Kg/m^2$(E: n=85;G: n=76) and $\geq$30 and $\leq 35 Kg/m^2$(E: n=75;G: n=84)were investigated. For BL BMI$\geq$25 to $\leq 30 Kg/m^2$,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$\geq$30 and $\leq 35 Kg/m^2$,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 -1.9kg was observed in E-treated pts with BL BMI $\geq$25 to $\leq 30 Kg/m^2$ 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 $\geq$30 and $\leq 35 Kg/m^2$ vs a weight gain of +2.3kg 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.