GLYCAEMIC AND WEIGHT EFFECTS OF EXENATIDE FOR DIFFERENT AGE GROUPS
Wintle M1, Guan X1, Brodows R2, Mac S1
1Amylin Pharmaceuticals, Inc, San Diego, CA, USA, 2Eli Lilly and Company, Indianapolis, IN, USA

OBJECTIVES: The incretin mimetic exenatide improves glycaemic control with associated weight reduction in patients with type 2 diabetes (T2DM) treated with metformin (MET) and/or a sulphonylurea (SU), or MET and/or a thiazolidinedione. As a drug's pharmacokinetics and pharmacodynamics can vary with age, we explored exenatide's efficacy and safety for patients <65 y and ≥65 y in this post-hoc analysis. METHODS: Patients completing ≥3 y of exenatide treatment on background therapies of MET and/or an SU (N = 217, age 58 ± 10 y, 64% male, weight 99 ± 18 kg, HbA1c 8.2 ± 1.0%, fasting plasma glucose [FPG] 9.6 ± 2.3 mmol/L, diabetes duration 8 ± 6 y; mean ± SD) had statistically significant (P < 0.05) mean (±SE) changes in HbA1c (−1.0 ± 0.1%), FPG (−1.3 ± 0.2 mmol/L), and weight (−5.3 ± 0.4 kg). The two subgroups (baseline age <65 y, N = 161, 53 ± 7 y, and ≥65 y, N = 56, 70 ± 4 y) differed in baseline duration of diabetes (7 ± 6 y, 11 ± 6 y). RESULTS: The mean (±SE) changes in HbA1c (−0.9 ± 0.1%, −1.2 ± 0.2%), weight (−5.2 ± 0.5 kg, −5.4 ± 0.6 kg), and FPG (−1.1 ± 0.3 mmol/L, −1.8 ± 0.3 mmol/L) were not statistically different for the two subgroups (all, P > 0.1). In patients completing 3.5 y of exenatide, changes in lipids for the <65 y subgroup (N = 118) and ≥65 y subgroup (N = 33) were not statistically different, as follows (mmol/L): HDL cholesterol (+0.21 ± 0.02, +0.25 ± 0.03), LDL cholesterol (−0.28 ± 0.09, −0.37 ± 0.15), total cholesterol (−0.26 ± 0.09, −0.33 ± 0.16), and triglycerides (−0.49 ± 0.17, −0.52 ± 0.14) (all, P > 0.2). Nausea and hypoglycaemia, the most common adverse events, occurred at similar rates in both subgroups. The only case of severe hypoglycaemia occurred in a patient <65 y whose background therapies were MET and an SU. CONCLUSION: In summary, in this open-label extension study of T2DM patients treated with MET and/or an SU, exenatide exposure ≥3 y resulted in similar safety profiles and improvements in glycaemic control and lipid concentrations, with associated weight reductions for patients ≥65 y and <65 y.

ADDITION OF INHALED HUMAN INSULIN AS AN OPTION FOR PATIENTS WITH TYPE 2 DIABETES UNCONTROLLED ON ORAL ANTIDIABETICS SHOULD AVOID COMPLICATIONS PREDICTED BY EAGLE MODEL
Littlewood K1, Whiteley J2, Mathieu C2
1Mapi Values, Houten, The Netherlands, 2Pfizer Inc, New York, NY, USA, 3Katholieke Universiteit Leuven, Leuven, Belgium

OBJECTIVES: The objective of this study was to compare the rate of micro- and macrovascular complications in type 2 diabetes mellitus (T2DM) patients, from increased insulin use due to the addition of inhaled human insulin Exubera (EXU) as a treatment option versus subcutaneous (sc) insulin alone using the Economic Assessment of Glycemic Control and Long-term Effects (Eagle) model. METHODS: The model included uncontrolled T2DM patients eligible for insulin. Long-term consequences were based on risk equations derived from DCCT, UKPDS and WESDR. The model used Freemantle’s estimates for year one. In the arm where EXU and sc insulin were available, 43% of patients initiated insulin therapy (35% inhaled and 8% sc insulin) versus 16% when only sc insulin was available. The subsequent yearly increase in insulin uptake was based on data from the DIN-LINK study. The model assumed 8% of patients remained on sc insulin. RESULTS: The mortality rate observed after 10 years was 34.5% versus 36.3% with inhaled and sc insulin versus with sc insulin respectively. Complications observed after 10 years, when inhaled and sc insulin were available vs. sc insulin alone, were 14.7% vs. 16.1% for myocardial infarction and stroke, 5.2% vs. 5.9% for proliferative retinopathy, 43.4% vs. 47.3% for microalbuminuria and 14.1% vs. 17.2% for clinical neuropathy. In sensitivity analyses, EXU’s advantages remained when insulin uptake was capped at 60% (i.e. always at least 40% on OADs). CONCLUSION: Delaying insulin initiation increases the rate of complications. The results showed that when insulin use is increased due to the availability of inhaled insulin, a reduction in all-cause mortality and the number of complications should be observed. Exubera has the potential to improve diabetes management by overcoming barriers to insulin initiation in T2DM patients, and could help prevent more long-term complications associated with T2DM.

EVALUATION OF THE ASSOCIATION BETWEEN GLUCOSE VARIABILITY, AS MEASURED BY THE DIFFERENCE BETWEEN MAXIMUM AND MINIMUM, INTERMITTENT, RANDOM BLOOD GLUCOSE OBSERVATIONS, AND LONG TERM CLINICAL OUTCOME IN SUBJECTS WITH TYPE 2 DIABETES TREATED WITH INSULIN
Piddle C1, Tyran A2, Currie C2
1Pharmatelligence Limited, Cardiff, UK, 2Eli Lilly and Company Limited, Surrey, UK, 3Cardiff University, Cardiff, UK

OBJECTIVES: The aim of this study was to determine if there was an association between random blood glucose (RBO) obser-