Differentiation of basal insulins in randomized clinical trials in T2DM subjects: a model-based meta-analysis of HbA1c and hypoglycemic event rates

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**Objectives:** To perform a model-based meta-analysis of HbA1c change from baseline and hypoglycemia event rates for basal insulins in T2DM subjects in order to evaluate differentiation amongst Standard of Care basal insulins.

**Methods:** A database of study-level aggregate data from published clinical trials for basal insulins and GLP-1 agonists in T2DM was constructed. The hypoglycemic event rate was classified consistently, namely all hypoglycemic events were classified as minor, except for major events, which required third party assistance, and nocturnal events, which occurred between 0:00-6:00 am. GLP1 agonists were included in the analysis to add a greater volume of placebo reference data. A longitudinal model was used to describe HbA1c over time as function of dose and baseline \([1]\). Mean drug effect models for minor, nocturnal, and joint minor+major hypoglycemia were developed and included exploration of a dose response model.

**Results:** Inclusion of GLP1 data enhanced stability of HbA1c and hypoglycemia model and precision of parameter estimates. HbA1c change data were well-described by a longitudinal dose-response model with covariate effects for baseline status, background therapy, body weight, and Japanese race. Hypoglycemia rate data were described equally well by a mean drug effect model and dose-response model using glargine as reference treatment. The final models were simulated independently by sampling 1000 parameter sets from the final parameter estimates with uncertainties (Figure). The major hypoglycemia rate for degludec was predicted to be approximately 85% that of glargine at clinical dose ranges.

**Conclusions:** MBMA models were successfully developed to describe hypoglycemia rate of basal insulins in Type-2 diabetes patient population. At the same HbA1c response, degludec has slightly lower, detemir equal, and NPH higher hypoglycemia rates than glargine. This analysis enhances understanding the differentiation potential of novel basal insulin treatment options.