APPENDIX 1

Each patient contributed one (if the patient did not experience a hypoglycemic event, or dropped out of the study after the first hypoglycemic event) or several episodes to the analysis. Each episode was split into intervals of one week, with $Y_{e,j}$ indicating whether a hypoglycemic event occurred ($Y_{e,j}=1$) during the j-th week of the e-th episode, or not ($Y_{e,j}=0$). The probability $h(j,X_{e,j})=Prob(Y_{e,j}=1)$ to experience an event was modeled as function of time (j) and covariates ($X_{e,j}$) using a log-log link function. More precisely, the model is $\ln(-\ln(1-h(j,X_{e,j})))= \alpha_0+\alpha_1 j+\alpha_2 j^2+\beta_1 HbA_{1c,ej}+\beta_2 HbA^2_{1c,ej}+\beta_3 1\{trt_e=glim\}+\beta_3 1\{sex_e=m\}$

where $HbA_{1c,ej}$ is the last measured HbA_{1c} value during week j and episode e, where $1\{trt_e=glim\}$ indicates whether the patient providing the data for episode e was treated with glimipiride (1) or vildagliptin (0), and $1\{sex_e=m\}$ indicating whether the patient was male. Parameter estimates for the α's and β's were obtained using all available data. The function $h(j,X_{e,j})$ was then plotted separately for the two treatment groups and week j=24 in Figure 1 for male patients. The third function for the glimepiride 2mg/day group in Figure 1 (and the functions in Figure 2) are obtained correspondingly, but now including separate indicators for glimepiride 2mg/day, glimepiride 6mg/day, and 'other' in the model. The hazard rate (HR) to compare vildagliptin with glimepiride was estimated as $\exp(\beta_3)$, and the corresponding unadjusted hazard rates were obtained using a model with $\beta_1=\beta_2=0$.

Parameter estimates were obtained using a covariance matrix with common correlation coefficient for all indicators $Y_{e,j}$ belonging to the same subject (irrespective of episode). We also explored additional covariates (e.g. age) and other models (with additional interaction terms) but none of these richer models provided a better fit to the data or indicated that the conclusions reported below would change with a different model.