Reviewer's report

Title: The consequences of delaying insulin initiation in UK type 2 diabetes patients failing oral hyperglycaemic agents: a modelling study

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Reviewer: Andreas Pfützner

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In general, this appears to be a well performed hypothetical modelling study regarding early use of insulin in patients with type 2 diabetes. The authors calculate a longer survival and later onset of diabetes complications in favor of early insulin use.

I have several comments:

There need to be some more clarification on the baseline model in the method section, or these points need to be discussed as limitations in the discussion section:

- what OADs were considered to be used instead of insulin in the late insulin group (co-medications in the UK in previously published trials may not necessarily represent current state of the art).

- The model is based on conventional therapy only - this needs to be more clearly stated

- according to the EASD guidelines early use of basal insulin is common in the EU (a factor limiting the transferability of the results into current practice)

- political company statements are not contributing to the quality of the paper and should be entirely left out. (E.g., the speculation regarding thiazolidinedione use and increased mortality in the ACCORD study in the discussion section: A. only rosiglitazone was used in ACCORD, B. all analyses show that mortality was not associated with TZD use in ACCORD, C. The whole discussion is questionable anyway because of study selection bias in the original meta-analyses. One could rather speculate that increased mortality in the intensive arm in ACCORD may have been induced by the high insulin doses leading to increased hypoglycemia frequency and stimulation of growth hormone effects by endothelial MAPK-1 activation, both factors contributing to an increased mortality).

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

In the past five years, I have received research support, consultancy fees, speaker fees and travel support from insulin producing companies (Eli Lilly, Sanofi-Aventis, NovoNordisk, Biodel, Halozyme, Mannkind, and Pfizer)