Reviewer’s report

Title: Predicting erythropoietin resistance in hemodialysis patients with type 2 diabetes

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Reviewer: Simeone Andrulli

Reviewer’s report:

Major Compulsory Revisions:

The paper of A. Schneider et al is a post-hoc analysis on data of 4D study. The aim of the study was to identify predictors for ESA resistance in diabetic hemodialysis patients. A number of putative predictors were explored from the area of clinical and routine laboratory parameters and of specific biomarkers. The conclusions of Authors were that “… Easily obtainable clinical parameters and routine laboratory parameters can predict ESA resistance in diabetic hemodialysis patients …. Specific biomarkers did not meaningfully further improve the risk prediction of ESA resistance. ….”

The paper is well written and easy to read. However, many aspects remained to clarify, as suggested in the comments:

1. The definition of ESA resistance is inflated and based more on statistical criteria than on clinical relevance. Defining the patients in the upper quartile as ESA resistant, the frequency of ESA resistance was extended, by definition, to 25% of enrolled patients. Moreover, the correspondent cut-off values were not given in the manuscript. I advice to give this information in table 1.

2. It is unclear whether the analysis is limited to the baseline data of the 4D study or whether the analysis is extended to the follow-up data.

3. It isn't mentioned how the authors managed the missing data that are likely distributed in a different manner among the explored predictors. For this reason I suggest to insert this information, variable by variable, in tables 1 and 2.

4. To give weight to this outcome variable, it should be advisable to explore its link with the primary outcome of the 4D study.

5. I advice to explore the percent iron saturation in place of the simple iron concentration in the blood.

6. In Table 1, there aren’t the values of the outcome variable of this study and of the some relevant predictors used in the models 1 (ace-inhibitors, heart rate), 2 (urea, potassium, iron and ferritin) and 3 (ADMA, PTH, 25OH vitamin D and osteocalcin).

7. In Table 2, please check the unit of measure of ferritin.

8. In Table 3, it is strange that the increase of urea concentration reduces the risk of ESA resistance. Moreover, the authors did not discuss why they hold the
predictors of model 1 in model 3, although they lost statistical significance. It is also strange that ferritin and CRP are not selected in models 2 and 3, respectively.

9. Figures 1-3 on ROC analyses are unnecessary because they can be replaced by only one row in table 3. This is relevant to obtain a more synthetic paper.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests