Reviewer's report

Title: Characterization of chronic and acute ESA hyporesponse: a retrospective cohort study of hemodialysis patients

Version: 3  Date: 4 April 2015

Reviewer: Massimo Torreggiani

Reviewer's report:

In this paper Sibbel and Colleagues aim to develop a valid definition of chronic hyporesponsiveness to erythropoisis stimulating agents (ESAs) in dialysis patients. They performed a retrospective study analyzing a database of a dialysis company that has more than 2000 dialysis facilities in the United States. Patients were followed from 15 months between February 2012 and April 2013. Their results show chronic hyporesponders were patients who did not respond to ESA therapy for at least four months. The same patients were transfused 7 times more frequently than acute hyporesponders and had a greater risk of death. Iron status did not seem to affect the responsiveness to ESAs.

Several comments might be addressed to this work.

Major Compulsory Revisions

- Definition of hyporesponsiveness to ESA is not clear. Beyond the ratio between hemoglobin and ESA dose, how hyporesponsiveness was define? How were the percentile thresholds defined to establish hyporesponsiveness in each stratum? Was it a discretionary choice of the Authors? Please comment or explain better.

- This paper lacks of statistics. Significancies are not expressed. The Authors should clearly state whether every parameter analyzed (demographics, Hb, ferritin, TSAT, etc.) is significant or not. For instance, in figure 2B there seems to be a great difference in TSAT at 4 months between acute and chronic hyporesponders and this is a matter of great importance in ESA resistance.

- Beyond the past medical history of the patients (Table 3-2), it would be important to know the clinical conditions of the patients at the time of the enrolling, for instance calculating the CIRS score.

- It would be useful to calculate mortality rate according to hemoglobin levels.

- How was the cut-off of 4 months to define chronic hyporesponsiveness determined? Is there a statistical analysis that supports this arbitrary definition or this assumption is based only on the appearence of the Kaplan-Meyer curve? If so, please clearly describe the statistical analysis, otherwise please comment.

Minor Essential Revisions

None

Discretionary Revisions
None

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests