Reviewer's report

Title: Plasma isofurans concentrations are associated with erythropoiesis-stimulating agent resistance in maintenance hemodialysis patients

Version: 2
Date: 10 December 2014

Reviewer: Lucia Del Vecchio

Reviewer's report:

The topic of this study is of interest and patient selection, together with experimental data collection are accurate. However, I feel that the statistical analysis should be modified.

Major Compulsory Revisions:

1) The major point is that by definition it is possible to talk of response to ESA only in treated patients. Indeed, observational studies have clearly demonstrated that the patients who do not receive ESA treatment have a far better outcome and different characteristics than ESA treated patients. Looking at table 1, I noticed that the majority of the patients with ERI <3.78 were untreated. For this reason the analysis should be performed after taking out untreated patients (you may consider them in a supplementary analysis).

2) Another point is antioxidant treatment. This is a randomised trial and thus the authors need to analyse the direct association among antioxidant treatment and both markers of oxidative stress and ERI.

3) More data should be added to Table 1. In particular, considering the possible factors influencing ESA response, information is needed on:
   - Serum albumin
   - Dialysis adequacy
   - PTH levels
   - Iron treatment
   - TSAT (this variable was used in the statistical analysis
   - Randomisation to study treatment

Minor Essential Revisions

1) The abbreviation HD is more widely used than MHD

2) The possible role of study treatment should be considered in the discussion section

-3) The patients enrolled in this study were younger and with a mean BMI higher than that commonly observed in everyday clinical practice. Please discuss the role of age and BMI on ESA response

- Discretionary Revisions
1) Discussion: there is an interesting study about carbamylate albumin and ESA hyporesponse. Please considering quoting and commenting it

**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:**

partecipation to an advisory board for astellas and takeda