**Reviewer’s report**

**Title:** In search of potential predictors of erythropoiesis-stimulating agents (ESAs) hyporesponsiveness: a population-based study

**Version:** 0  **Date:** 04 Mar 2019

**Reviewer:** Reviewer 2

**Reviewer’s report:**

PEER REVIEWER ASSESSMENTS:

**OBJECTIVE** - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

Yes - there is a clear objective

**DESIGN** - Is the current approach (including controls and analysis protocols) appropriate for the objective?

Yes - the approach is appropriate

**EXECUTION** - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

No - there are minor issues

**Statistics** - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

**INTERPRETATION** - Is the current interpretation/discussion of the results reasonable and not overstated?

No - there are minor issues

**OVERALL MANUSCRIPT POTENTIAL** - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions
PEER REVIEWER COMMENTS:

GENERAL COMMENTS: This is a large data based observational historic cohort study among incident ESA users of cancer and CKD patients, respectively. The aim was to identify factors that are associated with ESA hyporesponsiveness for the two patient populations.

The study ideas and presentation is clear. One of the important findings is that the type of dispensed ESA (biosimilar or originator) was not a predictor of ESA hyporesponsiveness in CKD.

REQUESTED REVISIONS:

Essentially, the study was conducted for two separate populations, i.e., cancer and CKD patients, so the p-values make little sense in Table 1 Characterization of incident ESA users at baseline. P-values as reported are to evaluate the balance of the characteristics of the two different populations. Baseline characteristics are incomparable between the two study populations. Suggest keep all summary statistics but drop all p-values from table 1. The study didn't intend to use one patient population as a comparison group for another.

ADDITIONAL REQUESTS/SUGGESTIONS:

Question/Suggestions to authors.

a) in Data Analysis section, what % of eligible patients whose indication for use were identified via the alternative algorithm? Plus, it is helpful to provide ESA average/median dose and duration in the time interval of ΔHb measurement if data permitted;

b) in Sensitivity Analysis section, should a 2x2 table be reported about the count of patients when ESA hyporesponsiveness were based on two different approaches, one was on ΔHb while the other on Hb>11? That would provide the info on the magnitude of exposure misclassification or consistence when two different definitions of EAS hyporesponsiveness were used.

c) in Statistical Analysis, strongly suggest reporting the Hosmer-Lemeshow goodness of fit tests for logistic regression models. ROC index cannot tell readers how well the models fit the data.

Note: This reviewer report can be downloaded - see attached pdf file.

Please confirm that you have included your review in the ‘Comments to Author’ box? As a minimum standard, please include a few sentences that outline what you think are the authors’ hypothesis/objectives, their main results, and the conclusions drawn. Your report should constructively instruct authors on how they can strengthen their paper to the point where it may be acceptable for publication, or provide detailed reasons as to why the manuscript does not fulfill our criteria for consideration. Please supply appropriate evidence using examples from the
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Yes

Are the methods appropriate and well described to allow independent reproduction of experiments?  
Please state in the ‘Comments to Authors’ box below what you think are the strengths and weaknesses of the methods (study design, data collection, and data analysis), and what is required, if anything, to improve the quality of reporting

No

Does the work include the necessary controls?  
If not, please explain in the 'Comments to Author' box below.

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Are you able to assess the statistics? 

- Are the statistical test(s) used in this study appropriate and well described?  

- Is the exact sample size (n) reported for each experimental group/condition (as a number, not a range)?  

- Are the description of any error bars and probability values appropriate?  

- Are all error bars defined in the corresponding figure legends?  

- Has a sample size calculation been included, or a description and rationale about how sample sizes were chosen?

Please can you confirm which of the following statements apply to your statistical assessment of the manuscript (Please include details of what the authors need to address in the ‘Comments to Author’ box):

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