Author's response to reviews

Title: Urine Neutrophil Gelatinase-associated Lipocalin to Predict Renal Response after Induction Therapy in Active Lupus Nephritis

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RESPONSE TO REVIEWER COMMENTS AND SUGGESTIONS

We thank the reviewers for their careful read and thoughtful comments on the previous draft, again. We have taken their comments into consideration in preparing our revision, which has resulted in a paper that is clearer, more compelling, and broader. The following summarizes how we responded to reviewers. We hope that these extensive changes, based on their critiques, make this manuscript suitable for publication in BMC Nephrology.

Reviewers' comments to Authors:

Editor

Editor Comments:

1) I and the reviewers agree that this is an interesting study. Please pay particular attention to the formatting and structure of the paper as per guidelines.

Authors’ response: Thank you for your suggestion. We have revised our manuscript follow the formatting and structure of the paper.

2) I agree with the reviewer 1 "exclude these 7 patients from analysis in order to have a homogeneous group in regard of active glomerular and intestinal lesions and to have more significant conclusions".
Authors’ response: Thank you for your suggestion. We have excluded patients with LN class V and also re-analysed in the revised manuscript.

3) Also, state the BMI instead of merely weight of the patients. I also recommend that the statistics need to be verified by a statistician.

Authors’ response: Thank you for your suggestion. We have added BMI in the table 1.

4) In addition, please do a thorough literature search in case you have missed any pertinent references.

Authors’ response: Thank you for your suggestion. We have added more references in that sentence.

Reviewer reports:

Khawla Kammoun (Reviewer 1):

1) This paper is about prediction value of urine NGAL in renal response after induction therapy in active lupus nephritis. It included 75 patients with biopsy proven lupus nephritis (LN) with predominantly class III or IV LN (isolated or associated to class V LN). 7 patients had isolated class V LN. In this study inclusion there is heterogeneity in inflammatory lesions because of inclusion of patients with isolated class V LN. We suggest to exclude these 7 patients from analysis in order to have an homogeneous group in regard of active glomerular and interstitial lesions and to have more significant conclusions.

Authors’ response: Thank you for your suggestion. We have excluded patients with LN class V and also re-analysed in the revised manuscript.

2) The authors report in the text that there was a trend toward higher levels of baseline GFR among LN with renal response than those without response: but the p value in very higher than 0.05. We suggest that there was no difference in GFR between the 3 groups.

Authors’ response: Thank you for your suggestion. We have corrected the following your suggestion as “there was no difference in GFR between the 3 groups”.

3) The authors found no correlation between urine NGAL and SLEDAI score. We suggest to study the correlation of urinary NGAL and isolated tubulointerstitial activity and chronicity scores and glomerular activity and chronicity score and glomerular scores.

Authors’ response: Thank you for your suggestion. Initially, we have analyzed in this point but there was no significant in the finding.

Gaetano La Manna (Reviewer 2): Please consider the following points we have identified:
1) According to Guidelines, the objective should not be included among abstract sections. It should be included in another section.

Authors’ response: Thank you for your suggestion. We have deleted the objective from the abstract.

2) As per our guidelines, please change "Materials and methods" section title with "Methods".

Authors’ response: Thank you for your suggestion. We have changed as your suggestion.

3) Conclusion session is required by the Editor for a research article. It should clearly state the main conclusions and provide an explanation of the importance and relevance of the reported study.

Authors’ response: Thank you for your suggestion. We have modified the conclusion as “In conclusion, this study indicates that NGAL in urine is one of biomarkers of the tubulointerstitial changes and perform better than conventional markers in predicting a clinical response to treatment of active LN. It may have the potential to predict renal response after induction therapy among SLE patients. Further investigation should focus on large populations with an analysis of urinary NGAL to find out whether NGAL can be used in clinical practice with higher sensitivity and specificity in predicting long term renal outcomes among SLE patients.”

4) As you can read from the instructions for Authors: "Manuscripts reporting studies involving human participants, human data or human tissue must include the name of the ethics committee that approved the study and the committee's reference number if appropriate".

Authors’ response: Thank you for your suggestion. We have corrected the Ethics approval and consent to participate as your comment.

5) In the abstract (line 39-40) please change "cuttoff" with "cut-off".

Authors’ response: Thank you for your suggestion. We have corrected.

6) Table 1: all the abbreviations should be preceded by the complete words the first time they are reported in the text. Please explain the meaning of acronym "ISN/RPS class".

Authors’ response: Thank you for your suggestion. We have added the complete words of ISN/RPS class in table 1.

7) Table 1 b caption: please clearly write that the parameter valuated among the three groups of patients is "urine NGAL to 24 urine creatinine ratio".

Authors’ response: Thank you for your suggestion. We have modified as baseline urinary NGAL to creatinine ratio (ng/mg Cr) among LN patients with renal response after induction therapy in Figure 1B.
8) Discussion session page 8 lines 21-22: please add reference to this sentence.

Authors’ response: Thank you for your suggestion. We have added more references in that sentence.

9) In section "Performance of urine NGAL in predicting renal response", page 8 line 7, you wrote: "...in differentiating complete and partial response groups THE from nonresponse group". Please remove "THE" from the sentence, it isn't necessary.

Authors’ response: Thank you for your suggestion. We have deleted “the” as your suggestion.

10) Page 7 lines 11-12: see note 9. Please remove "DID" from the sentence, it isn't necessary.

Authors’ response: Thank you for your suggestion. We have deleted “did” as your suggestion.

11) Page 9 line 1: Please remove comma from the sentence, it isn't necessary.

Authors’ response: Thank you for your suggestion. We have deleted “comma” as your suggestion.

12) Page 11 line 6: you wrote "The findings can be explained by the fact that urine CREATININE in acute kidney disease is a dynamic process affected by glomerular filtration and tubular secretion...". Please add the word "excretion" after creatinine.

Authors’ response: Thank you for your suggestion. We have added “excretion” as your suggestion.

13) Could the different numbers of patients for each subgroup influence the results?

Authors’ response: Thank you for your suggestion. It could be some effects on the results, however, our study included adequate sample size with significant outcomes as shown.

14) Shouldn't BMI be more significant than body weight?

Authors’ response: Thank you for your suggestion. We have added BMI in the table 1.