Peer Review File

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Review Comments (Round 1)

Comment 1: Statics: Was one-way ANOVA also used to compare the two groups? What about nonparametric data?

Reply 1: We used two-sample t-test to compare differences between the two groups. For nonparametric pairwise comparisons, we used the chi-square test.

Comment 2: Please specify the indications for biopsy in SLE patients at the authors' institution. How many patients initiated treatment prior to biopsy? Was there a difference in C3dg deposition or MAC deposition with or without treatment prior to biopsy?

Reply 2: The indications for biopsy in SLE patients in our center: all active lupus nephritis patients without treatment and serious contraindication will undergo renal biopsy. Once the diagnosis of systemic lupus erythematosus is confirmed, we will start to treat it according to the disease conditions. Before renal biopsy, there were fewer lupus patients who have not been treated. So it was difficult to compare the C3dg deposition or MAC deposition with or without treatment prior to biopsy.

Changes in the text: Line 62-63

Comment 3: What exactly is the "treatment outcome at 12 months" in the ROC analysis? Is it the degree of proteinuria, renal function, or what? If the authors want to show the superiority of C3dg and MAC over low C3 (and/or C4) in predicting disease activity, shouldn't they (C3dg, MAC deposition and low C3) be compared?

Reply 3: Thank you for your suggestion, we have revise in the text**.** Complete Renal Response (CRR) is defined as urinary protein creatinine ratio <0.5, eGRF was not more than 10% below the pre-flare value or >=90 mL/min/1.73m^2 and was not a treatment failure. Treatment aims for optimisation (preservation or improvement) of kidney function, accompanied by a reduction in proteinuria of at least 50% by 6 months, and a UPCR target below 500–700mg/g by 12 months (complete clinical response). We think that C3dg and MAC are different from C3 and C4 in blood, and tissue deposition is the most direct.

Changes in the text: Table 4; Line 184-189

Comment 4: Discussions: In the Discussion section, there is a lot of repetition of results and almost nothing is discussed. What can be derived from these results should be discussed further. For example, why does C3dg or MAC deposition exacerbate the disease? What are the mechanisms involved?

Reply 4: Thank you for your suggestion, we have modified the discussion part in the text.

Changes in the text: Line 216-222

Comment 5: Serum C3 is an indicator of disease activity in the entire SLE population, including patients with uncomplicated lupus nephritis, but can C3dg and MAC only be utilized in patients with lupus nephritis? Can the presence of C3dg or MAC deposits be evaluated outside of renal biopsy tissue? If not, then these would be clues to the pathogenesis of lupus nephritis rather than indicators of disease activity.

Reply 5: Thank you for your suggestion, C3dg and MAC are transmembrane sediments, mainly concentrated in renal tissue, the presence of C3dg or MAC deposits would be clues to the pathogenesis of lupus nephritis rather than indicators of disease activity.

Changes in the text: Line 235,245

Comment 6: Line 123, Line 140, and Tables: Age and serum creatinine values to one decimal place are sufficient. There are several other values that are good to one decimal place, so please check them out.

Both MAC and Mac are used within the manuscript. Since membrane attack complex (MAC) is defined at the beginning, it should be unified to it.

Line 176: “cell crescent” should be “cellular crescent”.

Table 4: For Response to therapy, either 'no' or 'yes' is sufficient.

Reply 6: Thank you for your suggestion, we have made changes in the text.

Comment 7: It is unclear the novelty of this MS. What points are novel and informative? This issue should be clearly explained.

Reply 7: Thank you for your suggestion, due to the importance of complement binding fragments in the LN, our center began to detect C3dg and MAC in kidney tissues from 2018. In this research, we summarized the data of the past years. It is novel to combine pathology with clinical data.

Changes in the text: Line 209-210

Comment 8: The tables are too confusing and complex. This issue should be resolved concisely.

Reply 8: Thank you for your suggestion, we have made changes in the text.

Changes in the text: Table 2

Comment 9: Are there any significance and implication of the examination of those molecules' deposition in addition to conventionally used histologic scores? This issue should be clarified.

Reply 9: Thank you for your suggestion, we have made changes in the text.

Changes in the text: Line 216-222

Comment 10: I do not think those molecules' deposition predicts the severity of the disease. The deposition may be sequelae of the severity of LN. This point should be clearly explained.

Reply 10:.Thank you for your suggestion, we have made changes in the text.

Changes in the text: Line 245,247

Review Comments (Round 2)

Comment 1: I understand the authors' response. Although the revised MS is much improved, some concerns still remain.

It is unclear the implication of their study in addition to previous histologic markers of the severity of lupus nephritis.

Unfortunately, this issue remains still. The limitations of the study should be stated clearly.

Reply 1: We used.