Author's response to reviews

Title: Infusion of autologous bone marrow mononuclear cells leads to transient reduction in proteinuria in treatment refractory patients with Idiopathic membranous nephropathy

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Reviewer #1

Why there was such great variation in the number of the injected mononuclear cells. Considering that variability why the authors did not choose to inject two different fixed amounts.

……This has been our experience that bone marrow aspiration leads to variations in numbers of cells obtained. We injected the entire amount that was retrieved and not a specific dose. Moreover, this was a pilot study with a small number of patients. We agree that going forward, a more standardised approach would be required.

"p" values for albumin and creatinine are missing in the manuscript text.

….. p values have been provided.

Did the authors look for differences in the histology or immunohistochemistry features of biopsies that could be correlated to the treatment response?

……. We did not specifically look for those parameters in this small number of cases. However, from our past experience, histological as well as immunohistochemistry parameters do not influence the response to therapy.

Do the authors could identify some special characteristics in the two patients with > 50% response?

…….No, we could not identify any special characteristics in these cases.

Reviewer #2

We appreciate the points made by the reviewer about the inclusion criteria and
whether the patients were truly treatment refractory or not. Some confusion has arisen because of the fact that for the inclusion criteria the proteinuria value was g/day/1.73m² body surface area (BSA), whereas the values shown in the graph are the actual values without being corrected for BSA. Our apologies for this confusion. The mean proteinuria value shown in the table is also after correction for BSA. We have now added another row showing the actual daily protein excretion values. The percentage reduction in proteinuria is based on actual values at baseline and at different time points, without correction for BSA.

For the sake of clarification, we are enclosing a spreadsheet containing the actual values of proteinuria, serum albumin and serum creatinine for the 11 patients who completed the study. The BSA and the baseline proteinuria/1.73m² has also been shown. This is meant for the reviewers only. We would like to reiterate (as already mentioned in the manuscript), all patients exhibited manifestations of a full-blown nephrotic state, with edema requiring regular diuretics, statins and had other complications such as infections and thromboembolic complications. As you will note from the spreadsheet, there is only one case who would not meet with the proteinuria/serum albumin inclusion criteria. However, in addition to being oedematous, this patient had experienced two episodes of venous thrombosis, the last about 3 months ago. Therefore, we believe the patients were truly refractory and needed treatment.

Unfortunately we do not have any values of cytokines/ T-cell counts in the patients.