Author’s response to reviews

Title: Allogeneic mesenchymal stem cell as induction therapy to prevent both delayed graft function and acute rejection in deceased donor renal transplantation: study protocol for a randomized controlled trial

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Version: 2 Date: 22 Oct 2017

Author’s response to reviews:

Dear editor,

Re: Manuscript No. TRLS-D-16-00761

Allogeneic mesenchymal stem cell as induction therapy to prevent both delayed graft function and acute rejection in deceased donor renal transplantation: study protocol for a randomized controlled trial

Thank you for the helpful comments on the above manuscript, which we have revised accordingly. Enclosed please find our revision and the point-by-point reply (in blue) to the recommended information.

We look forward to hearing from you.

Yours sincerely
Reviewer’s comments:

Reviewer #1: I tried to read carefully the paper "Allogeneic mesenchymal stem cell as induction therapy to prevent both delayed graft function and acute rejection in deceased donor renal transplantation: study protocol for a randomized controlled trial" but I was disappointed that the authors did not follow the SPIRIT recommendations. I just comment 3 examples bellow.

1) The SPIRIT figure should highlight that recruitment precedes allocation. Please divide the first column of your spirit figure in 2 columns (please, consider avoiding overlapping information between this figure and table 1).

Our reply:

We are grateful for your kindly comments. We have revised a new SPIRIT figure named Figure 1 to summarize enrollment, interventions, assessments, and timing for measurements in the Study design section.

2) Although your Spirit table states that sample size rationale is explained in page 8, the only provided information is just that the number of cases per group is 50, but you do not justify the reasons for this number. Please, see examples in the SPIRIT explanatory document. [Additionally, it is not clear to me what "stage" means, since figure 1 shows them as different 'arms' of the trial. Please, note this flowchart is a Consort figure, to show losses during trial conduct, but not the design of the trial. Please, consider dropping it.]

Our reply:

We are grateful for your kindly comments. We have added the sample size section in page 13, 14. The sample size was calculated based on our previous data showing that there was no BPAR in MSC treatment group at 6 months after transplantation, compared with 16.7% of acute rejection in the control group[Peng Y, Ke M, Xu L, Liu L, Chen X, Xia W, et al. Donor-derived mesenchymal stem cells combined with low-dose tacrolimus prevent acute rejection after renal transplantation: a clinical pilot study. Transplantation.2013;95(1):161-8]. Based on this preliminary study, we calculated that 44 patients per arm would be required to achieve a power of 90% with a two-sided significance level of p < 0.05. To account for possible dropouts (10%), the target number of patients was, therefore, set at 50 per arm (100 in total). We also prepared a document named ‘the additional file1’ to justify the reasons for this number.

3) Please, to prevent selective outcome reporting, specify the main outcome and the main statistical analysis, maybe with the help of an additional statistical analysis plan. [Additionally, please note that ITT, nor mITT are no more recommended populations. Please, read carefully the
SPIRIT or the CONSORT statements and do your best to avoid missing data. Please consider useful advice to prevent it at http://www.nejm.org/doi/full/10.1056/NEJMsr1203730.

Our reply:

We are grateful for your kindly comments. In the Methods/design section, we added the primary and secondary endpoints of this trial in page 7. To prevent selective outcome reporting, we consulted with an additional statistical analysis, and revised the ‘Statistical analysis’ section to achieve more accurate in page 14, according to a revised SPIRIT Checklist.