

Round 1

Dear Reviewer,

Thanks for your time and valuable input.

❖ Considering point 1 and 2:

Studies in table 4 represent all the published RCTs that evaluated maintenance steroid protocol versus a steroid-free approach over the past two decades without any selection bias.

The decision to include RCTs published over the past two decades only was to summarize the latest published data while considering the optimal size and word count of our review article.

❖ Considering point 3:

I think the Reviewer was asking about table 2 (in the initially submitted form), which describes a retrospective analysis of UNOS data system estimating the safety of steroid withdrawal in African American recipients.

Despite being a retrospective analysis of UNOS data, it is still worse mentioning it included a large number of patients (5565 black kidney transplant recipients) with 10 years follow up.

We acknowledge the inherited limitations of retrospective studies (such as lack of proper randomization, and the inability to exclude unrecognized confounders). That is why we did not include this article in our RCT table.

❖ Considering point 4 and 6:

I agree with the Reviewer that there is no clear answer to these points. Nevertheless, I think the introduction of MMF and tacrolimus had allowed the use of a low dose of maintenance steroids, which was reflected in fewer steroid-related complications and made total steroid avoidance a less demanding target.

❖ Considering our steroid-free practice:

Our clinical practice is steroid tapering to reach 5 mg of oral prednisolone by 24 weeks post kidney transplantation. Steroid-free approaches were used on an individual basis (whenever the steroids are contraindicated or not tolerated). We

aimed to conduct this review to assess the published evidence for our future regular use of the steroid-free protocol.

➤ Important note:

Table 1 and 2, together with figure 1 in the initially submitted manuscript, were removed due to the inability to get written approval from the reference articles publisher. No other changes were done to the remaining manuscript.

Round 2

The comments on the second-round review were noted. We agree with the reviewer's analysis in the first review that most of these queries do not have a right or clear answer. Our article tried to summarize the enormous scientific material covering this debatable topic, keeping in mind that no solid recommendations or guidelines are available to date regarding any of the steroid withdrawal approaches. Nevertheless, after reviewing all the presented RCT articles, we developed a strong belief that steroid-free protocols should have different shapes and forms taking into account patient variables (age, ethnicity, medical background, HLA mismatches, immunological risk stratification, etc.), and it can offer a comparable outcome with a lower burden of associated co-morbidities.

I have modified the conclusion of our article to include the points mentioned in the coloured paragraph. The new and revised manuscript was uploaded to the site under the topic reply to the author under the name of "61030-Manuscript-Second revision". I also attached a copy to this email. I am also ready for any further modifications required.