

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The article is within the scope of the magazine and deals with an interesting topic. It is well written and organized. Reading is fluid. A well-designed experiment is presented and the results are discussed. The contribution is original and novel, and represents an advance in the area of knowledge. However, some aspects should be improved: a) The state of the art should be expanded in the field of the experiment. b) The materials and methods used should be explained.

Response to reviewer 1 comments:

a) The state of the art should be expanded in the field of the experiment. → Dear reviewer, thanks for the comment. We have covered the majority of the experimental findings of ATG research in the “Discussion” section of the review.

b) The materials and methods used should be explained. → Dear Reviewer, thanks. We have mentioned the methods from lines 50-55 on page 2. “For this review, we studied peer-reviewed research articles published in PubMed-indexed journals. We reviewed the various clinical trials of ATG, its use in treatment of acute rejection, steroid-resistant rejection, and recurrent rejections and clinical studies published in similar journals. We excluded reports presented as conference abstracts and those published in languages other than English.”

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Rejection

Specific Comments to Authors: Thanks to the authors: I have the following points: 1. I didn't find a new message from this mini-review. Even it fits the design of a literature review rather than a narrative review manuscript. Furthermore, there is no description of how they reviewed the literature. 2. It needs restructuring and better subheadings with proper descriptions and evidence under each one. The thoughts are mixed between different categories, like the mechanism of action, dosing, etc. 3. Even when they described the triple maintenance therapy, they missed the well-described SYMPHONY Trial, which consolidated the evidence about Induction therapy with ATG and Maintenance with TAC+MMF+PRD. 4. There are many redundancies in the writing. 5. There is no actual proper definition of steroid-resistant Acute TCMR. 6. The authors referred to the study by Hanaway et al. (Ref Number 33, NEJM 2011). They used the study's conclusion of using Alemtuzumab as induction compared to ATG and Basiliximab. They converted it as a treatment for acute rejection!! 7. It would be great if authors added data about the emerging evidence of Anti ATG Antibodies, which is one of the causes of failing ATG therapy and how it should be tackled. 8. There should be a special topic about ATG resistant ATCMR.

Response to reviewer 2 comments:

1. I didn't find a new message from this mini-review. Even it fits the design of a literature review rather than a narrative review manuscript. Furthermore, there is no description of how they reviewed the literature. → Dear reviewer, thank you for the comment. Our review highlights the challenges faced by clinicians when navigating the available literature to strike the optimal balance between the risks and benefits of ATG utilization in renal transplantation. We have tried to cover research studies that are relevant to our review topic. For the method of literature review, we have written it from lines 50-55 on page 2. "For this review, we studied peer-reviewed research articles published in PubMed-indexed journals. We reviewed the various clinical trials of ATG, its use in treatment of acute rejection, steroid-resistant rejection, and recurrent rejections and clinical studies published in similar journals. We excluded reports presented as conference abstracts and those published in languages other than English."

2. It needs restructuring and better subheadings with proper descriptions and evidence under each one. The thoughts are mixed between different categories, like the mechanism of action, dosing, etc. --> Thanks for the comment. We have changed our review title to "Anti-Thymocyte Globulin (ATG) for Treatment of T-Cell-mediated Rejection in Kidney Transplantation". We did not change the subheadings as we think this is appropriate for the content we wrote. However, we have revised all the contents to have a clear message rather than mixed.

3. Even when they described the triple maintenance therapy, they missed the well-described SYMPHONY Trial, which consolidated the evidence about induction therapy with ATG and Maintenance with TAC+MMF+PRD.--> Dear reviewer, thanks. We added the SYMPHONY trial which is in lines 235-237 on page 8. "The landmark Symphony trial consolidated evidence for reduced exposure to calcineurin inhibitors in kidney transplantation, in conjunction with induction with daclizumab, MMF and corticosteroids"

4. There are many redundancies in the writing.--> Thank you for the comment. We have reviewed the article for redundancies. We have eliminated the redundancies.

5. There is no actual proper definition of steroid-resistant Acute TCMR. → Dear reviewer, thanks for the comment. The definition of steroid-resistant acute TCMR is written in lines 146 to 150 on page 6. "In approximately 25 to 30% of the patients, rejections are not reversed with steroid therapy alone. In these recipients, more intensive immunosuppressive therapy is required to reverse the AR episode. When serum creatinine levels do not recover to within 120% of the pre-rejection baseline value following corticosteroid pulse therapy within 14 days of the steroid medication's initiation, the episode is deemed steroid resistant"

6. The authors referred to the study by Hanaway et al. (Ref Number 33, NEJM 2011). They used the study's conclusion of using Alemtuzumab as induction compared to ATG and Basiliximab. They converted it as a treatment for acute rejection!! → Dear reviewer, thanks. We have removed this study from the review.

7. It would be great if authors added data about the emerging evidence of Anti ATG Antibodies, which is one of the causes of failing ATG therapy and how it should be tackled. → Thank you. We have added this in line 291-292 of page 10. "Lastly, role of anti-ATG antibodies and their role in negating therapeutic potency of ATG needs to be established"

8. There should be a special topic about ATG resistant ATCMR.--> Dear reviewer, thank you for the comment. We believe that ATG resistant ATCMR is not relevant for this review.

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: I compliment the authors, the article is well written, only minor style problems such as using the term "alteration" (better to use change, for instance). The section "Treatment of T Cell-Mediated Rejection" should include and comment on randomized trials addressing the subject.

Response to reviewer 3 comments:

Dear reviewer, thank you for the comment. We have commented on randomized trials and further summarized them in Table 1.