

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Transplantation

**Manuscript NO:** 56747

**Title:** Exploring the safety and efficacy of adding ketoconazole to tacrolimus in pediatric renal transplant immunosuppression

**Reviewer's code:** 00503176

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Croatia

**Author's Country/Territory:** Guatemala

**Manuscript submission date:** 2020-05-15

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-05-15 13:59

**Reviewer performed review:** 2020-05-15 14:24

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

I have reviewed the article 56747. It reports on a topic that is of interest considering the patient population (ESRD children-renal transplant recipients) and the setting (LMIC); and the strategy in question. The article is well written and clear. still, some minor revisions are needed (in my opinion). 1. Still some English polishing is needed (and there are a few typos scattered across the manuscript). 2. I understand that it is accustomed to provide "statistical tests" - but here, this is really NOT needed (i.e., pre-post t-test). It would be more informative to provide pre-ketoconazole values, post-ketoconazole values (as they already are reported) - and DIFFERENCES (with 95% CIs) between post- and pre-values. P-values really are not relevant here - a more important information is the AMOUNT of CHANGE (numerically provided). 3. A few things need to be additionally clarified: a): tacrolimus levels: when you say "median concentration"..what do you mean? Median trough concentration? or...?...The same with "minimum". In the methods section you should describe timing of blood sampling for tacrolimus concentration measurements. and clearly specify what do the reported numbers represent. 4. Table 1(or maybe one additional table) would be much more informative if it could include: a) liver transaminase levels (by time-point) b) information about time-span between pre-ketoconazole visits and time-span after inclusion of ketoconazole...so that one can have an idea about the time elapsed between the reported values. 5. Finally - are there any other children who were NOT switched to ketoconazole?...The whole point that you would like to make would be much stronger if you could included a cohort (it does not matter whether it is small) of children who at that time ("in parallel" to the 25 reported children)...were kept constantly WITHOUT ketoconazole (and .e.g, provide...data on doses, concentrations, liver transaminases from control checks taken during an approximately similar time-period as for the reported



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cohort).

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**Reviewer's code:** 00503195

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Associate Professor, Professor

**Reviewer's Country/Territory:** Greece

**Author's Country/Territory:** Guatemala

**Manuscript submission date:** 2020-05-15

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-05-15 17:17

**Reviewer performed review:** 2020-05-15 17:56

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

The study is interesting and showed that the addition of a small dose of ketoconazole minimizes the required dose of tacrolimus with safety. The latter is particularly important in low-income countries or low-income populations. The originality of the study is that it evaluated a pediatric population. Currently, there are no signs for improvement of the financial situation in many developing countries or in for attenuation of vast economic inequalities in certain other countries. Thus, the findings of the study could be characterized as significant. Comments In the statistical analysis, it may be more proper to use the paired t-test.

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**Reviewer's code:** 00503257

**Position:** Editorial Board

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** Guatemala

**Manuscript submission date:** 2020-05-15

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-05-16 00:49

**Reviewer performed review:** 2020-05-16 01:03

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
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#### **SPECIFIC COMMENTS TO AUTHORS**

Although this MS may be somewhat interesting, it remains only anecdotal clinical experience. 1. Follow-up duration in each patient remains too short to draw any conclusion regarding the efficacy and safety of authors' protocol. 2. Sample size is too small to draw any conclusion. 3. Some tables or figures which describe authors' protocol clearly are needed. \$ The title of the MS is strange.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Reviewer's Country/Territory:** Croatia

**Author's Country/Territory:** Guatemala

**Manuscript submission date:** 2020-05-15

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2020-08-06 06:04

**Reviewer performed review:** 2020-08-06 06:18

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS



The language was one of the main limitations of the original submission. It has been greatly improved. The overall presentation of intention of the work, the flow and data presentation has been much improved. I have no further comments to authors.

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**Author's Country/Territory:** Guatemala

**Manuscript submission date:** 2020-05-15

**Reviewer chosen by:** Jin-Lei Wang

**Reviewer accepted review:** 2020-08-06 09:03

**Reviewer performed review:** 2020-08-06 09:11

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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## SPECIFIC COMMENTS TO AUTHORS

The authors did the requested improvements.