

Hamburg, April 04th 2021

Answers to reviewers

Estimated colleagues,

Thank you for reviewing our manuscript and giving us both interesting and helpful suggestions and information as to where and how we can improve our work.

We carefully considered all of the major and minor comments and will answer point by point. Also, we reviewed the manuscript by the suggested format and content reviewing guidelines. An article highlight section has been added to the manuscript. We updated the reference format according to the guidelines.

We reviewed tables and figures and will attach them as wished in separate documents. Finally, the entire manuscript was reviewed once more by our language editor (who is a native speaker) Prof David Tracey.

Major & minor comments:

The study cohort was not homogeneous

In order to not provoke a selection bias by excluding patients with multiple LTs or patients with extremely short or long times of 'graft survival', we kept these patients in our study cohort. On the contrary, analyzing different outcomes after LT regarding the topic of the impact of DSA on graft survival, was one major objective of this study. We felt that the heterogeneity of study participants is representative for the heterogeneity of patients we see in our follow-up examinations.

As it was a retrospective cohort study, it was inevitable to avoid downsizing our study cohort since there was a certain amount of missing data. Since providing a statistical comprehension of the previously described DSA-impact on graft survival was one aim of the study and in order to keep the study within the possibilities of valid statistical analysis, we were very critical in deciding if a patient was suitable for inclusion into the cohort. We made individual decisions after carefully studying each patient's history and follow-up compliance. If a patient did not meet basic criteria for study inclusion, she or he was excluded.

Please also see page 11/12 of the paper, where we also discuss the limitations of this retrospective study.

Liver enzymes in rejection biopsies

We do agree that the presence of normal liver enzymes in patients with histological signs of rejection is an interesting finding and also agree that it is worth discussing more in depth. Therefore, we added a section to our discussion, where we discuss the topic of silent immune-mediated allograft injury. Please find a new reference by Ohlsson et al added to the reference list. We also talk about it in our conclusion and therefore hope to be able to provide a strong message for clinical practice to the reader.

Thank you for suggesting to add the numbers at risk to our figures. You will now find them in the footnotes / figure legends. We also added reason of graft loss to Table 1. The adherence to immunosuppression can be found in Table 2.

Regarding the figures: We can provide different formats if needed: .pdf, .tif, .eps, .png and we can also add/edit footnotes and legends/title if desired.

As recommended, we provide the consent form, ethics statement and biostatistic review statement in higher resolution.

You will also find the copyright license agreement signed by all authors (including the most recent contributor Dr. Beime) and the conflict of interest statement signed by our corresponding author PD Dr. Grabhorn.

We are very happy to hear about your conditional approval and hope to be able to fully meet your revision wishes.

Sincerely

F. Schotters and E. Grabhorn



ANSWERING RE-REVIEW REPORT

Name of journal: World Journal of Hepatology

Manuscript NO: 61431

Title: Impact of donor-specific antibodies on long-term graft survival with pediatric liver transplantation

Reviewer's code: 03668558

Position: Editorial Board

Academic degree: MD

Professional title: Consultant Physician-Scientist, Doctor

Reviewer's Country/Territory: Italy

Author's Country/Territory: Germany

Manuscript submission date: 2021-01-25

Reviewer chosen by: Han Zhang (Part-Time Editor)

Reviewer accepted review: 2021-04-13 05:37

Reviewer performed review: 2021-04-13 05:55

Review time: 1 Hour

Scientific quality	<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
Language quality	<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
Conclusion	<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 Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
Peer-reviewer statements	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

The Authors fairly answered my previous comments. In my opinion, the issue of patients' selection remains, but it has been discussed in the appropriate section. Prospective data on this interesting topic will strengthen these findings. I do not see in Table 2 and Table 1 causes of graft loss and adherence rate.

ANSWERING REVIEWERS

Estimated Editors and Reviewers,

we are happy to hear our work was recommended for publication and would like to thank you for your interest in our work and for your constructive comments in this second round of review. In this document, we try to address the issues raised as best as possible.

"In my opinion, the issue of patients' selection remains, but it has been discussed in the appropriate section."

We are happy to hear our revision work was approved and contributed to resolving some of your concerns regarding the patient selection.

"prospective data is needed to strengthen these findings"

We agree with the reviewer and wouldn't want to overstep our current results. Therefore, we also plan to conduct longitudinal analysis in the future.

"I do not see in Table 2 and Table 1 causes of graft loss and adherence rate."



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Thank you for suggesting adding clarifying information to our Tables. We included causes of graft loss to Table 1 and adherence rates to Table 2. You will find them highlighted in yellow.