ANSWERING REVIEWERS

May 8, 2017

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 34093-1-revised_cleancopy.docx).

Title: Gut barrier failure biomarkers are associated with poor disease outcome in patients with primary sclerosing cholangitis

Author: Tamas Tornai, Eszter Palyu, Zsuzsanna Vitalis, Istvan Tornai, David Tornai, Peter Antal-Szalmas, Gary L. Norman, Zakera Shums, Gabor Veres, Antal Dezsofi, Gabriella Par, Alajos Par, Peter Orosz, Ferenc Szalay, Peter Laszlo Lakatos, Maria Papp.

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 34093

We are grateful to the reviewers for their positive opinion, useful recommendations and for suggesting our paper for publication. The manuscript has been improved according to the suggestions of reviewers and editor.

Answers to editor's comments:

1. We provided the revised manuscript in two formats (34093-revised-clean copy.docx, 34093-revised-highlighted.docx)
2. We provided the supporting documents in PDF format regarding the approved grant application forms, ethics approval, informed consent statement and conflict-of-interest statement, Conflict-of-interest statement, Data sharing statement, Grant application forms, Language certificate at first submission.
3. We added audio core tip in the appropriate format (.mp3).
4. We wrote "Scientific Research Process" form according to the editor's guidelines.
5. We wrote the "Comments" section according to the editor's guidelines.
6. We answered the reviewers' comments, and added it to "Peer-review" section.

Answers to reviewer comments:

Reviewed by 00004594

"This is an original and interesting manuscript. The data are convincing for me. Regarding the AGA, these antibody are no more reimbursed in France for example and perhaps in other countries"

Thank you for your comments. Anti-gliadin antibodies (AGA) are available in Hungary, both in the private and the public sectors of health care. Their use however, is mainly limited to the

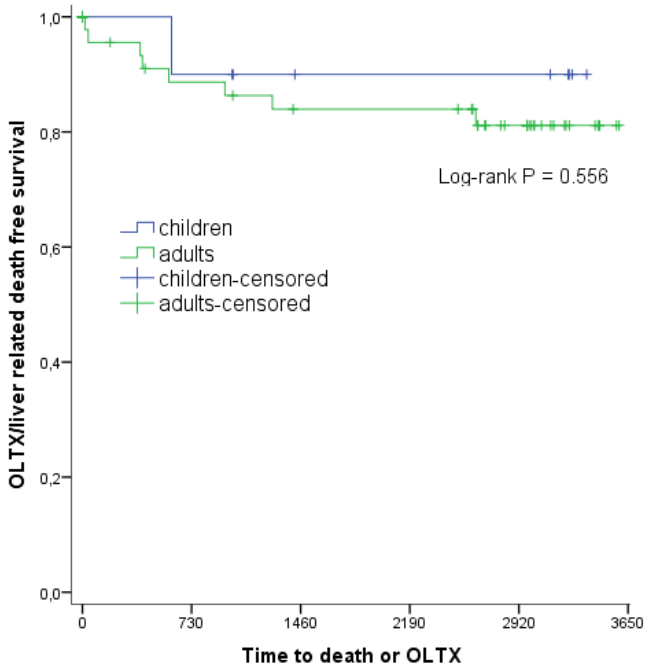
diagnostic workup of food intolerance. IgA type AGA was not frequent in PSC in our cohort, only 9% (6/67).

Answers to reviewer comments:
Reviewed by 03669108

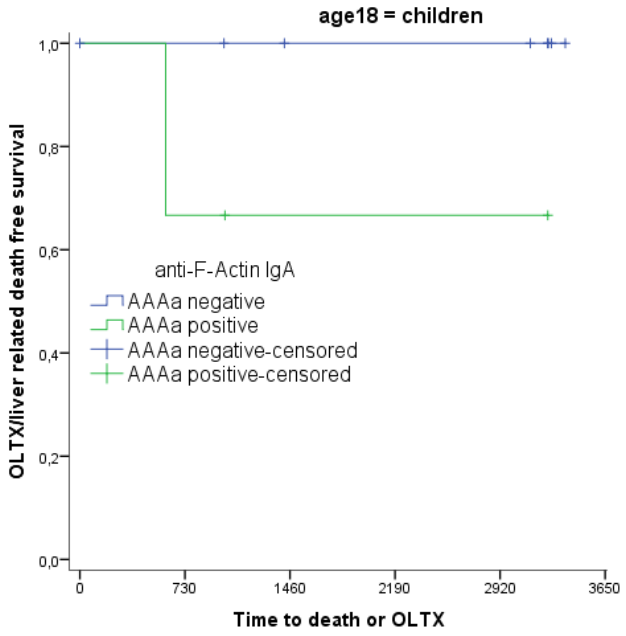
"A very good article, in my opinion, with only one problem: including children and adults, although we know that both diseases (PSC and BD) are having special features in children."

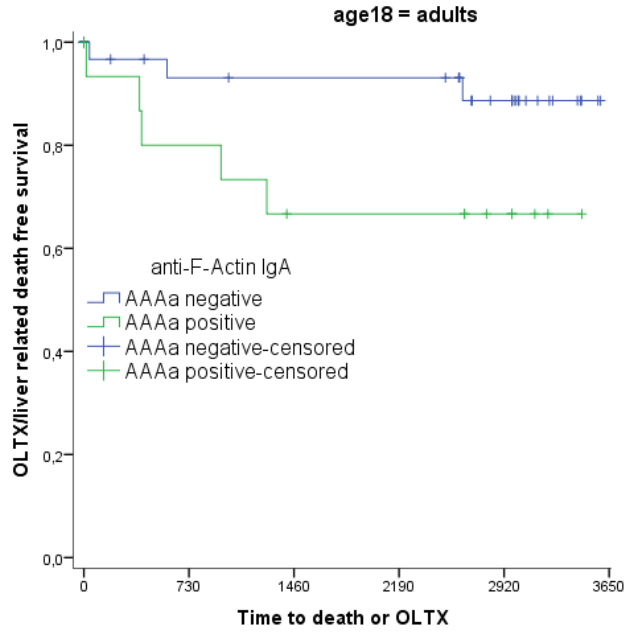
Thank you for your comments.

We agree that PSC in children and adolescents have somewhat different clinical presentation. This includes laboratory abnormalities, and concomitant autoimmune liver disease. However survival differences were not compared head to head in recent investigations. The largest study to date including more than 700 pediatric PSC patients show a 10 year transplant free survival rate of 70% (95CI:65-74%) (Deneau MR, Hepatology, 2017 Apr 8 [EPub]) and is similar to that observed in adult patients (~75%) in a recent population based study from The Netherlands (Boonstra K, Hepatology, 2013;58;2045-55). Tertiary care centers report lower transplant free survival, probably reflecting the referral of more seriously ill patients for evaluation for liver transplantation (Lazaridis KN, NEJM, 2015;375;1161-70). As for our cohort of patients, we have shown that age at diagnosis and disease duration was not different according to antibody status (**Table 3**). Transplant-free survival according to age groups was also not different in this Hungarian PSC cohort. We provide Kaplan Meier curves for the reviewer comparing survival with native liver according to age group.



Additionally we show the result of the stratified Kaplan Meier procedure according to age groups.





English language editing was performed by a native English speaker. Certificate is attached as well.

Linguistic edits and other changes in the content of the text were highlighted **in red**.

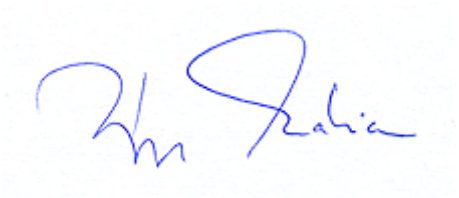
Please find attached the "highlighted" version of the manuscript with the detailed changes that were made according to the reviewers' comments.

We would like to thank you again for the helpful comments and for considering our paper.

All authors have fulfilled the criteria of authorship and seen and approved the final version of the revised manuscript and they have authorized the first author to grant on behalf of all authors to transfer exclusive copyright to World Journal of Gastroenterology in case of acceptance.

We do hope that the new data presented could be of interest to the readers of the World Journal of Gastroenterology.

Sincerely yours,



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