Author's response to reviews

Title: Analysis of the clinical relevance of antimitochondrial antibodies to the beta- and gamma-subunits of the F1F0-ATPase in patients with primary biliary cirrhosis

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Author's response to reviews: see over
Sir,

enclosed our revised manuscript “Clinical relevance of antimitochondrial antibodies to the \(\beta\)- and \(\gamma\)-subunits of the \(F_1F_0\)-ATPase in patients with primary biliary cirrhosis” by Nann et al (MS 1085227577747842).

We are very grateful for the helpful comments by the reviewers and revised the manuscript as follows:

**Reviewer 1**

1. Table 4 was omitted and instead in fig 4 individual values were added
2. Fig 1 includes only data from the 59 patients before any therapy. The fig. was reconstructed as scatter blot and individual values plus median are now shown.
3. There was no correlation between anti-\(\beta\)/\(\gamma\)-antibodies and anti-PDC-E2 antibodies, and this was added in 'results'.
4. The ROCs are added as supplementary data.

**Reviewer 2**

1. We completely agree that for the demonstration of anti-M2/ODC antibodies it is very important to use an antigen fraction containing the most relevant E2-subunits of ODC. This is just the reason why we employed the M2-antigen prepared from bovine heart mitochondria because it contains all five determinants of the ODC as already outlined in several publications, and in our experience their content does not vary significantly between different preparations. Nevertheless, all anti-M2 negative PBC patients were tested by Westernblotting against the recombinant antigens but revealed again negative results. These data were added in 'patients'.
2. We did not mention this point in detail because this discrepancy has already been discussed in our previous publication (Feuchtinger et al, 2009; Preuß et al, 2012). But we added some words on this in the discussion.

3. Fig.1 was reconstructed as a dot blot and median values are given. Other controls than healthy have not been added in this paper because the data have recently been published (Preuß et al, 2012).

Reviewer 3

1. The terms anti-β and anti-γ was introduced in the abstract and the introduction.

2. We did not mention the controls because we have already published these data (sera from patients with different autoimmune and non-autoimmune liver disorders and rheumatic diseases) in a previous paper (Preuß et al, 2012). But we clearly stated in the introduction that the anti-beta and gamma-antibodies are not strictly PBC specific, but nevertheless we wanted to analyse their clinical relevance in PBC in order to see whether they may be indicative for a distinct subgroup of PBC patients or an association with another disorder.

3. Data on ANA are added in table 1 and in an additional paragraph in ‘results’.

4. The correlation between antibodies detected by IFT and ELISA was added in an additional paragraph in ‘results’.

5. The numbers in fig. 3 and 4 were added. For the UDCA patients we now included into the analyses only the patients being anti-β/γ-positive and present the data in a figure. The figure for MTX-data was omitted and results were only mentioned in the text. After exclusion of the anti-β/γ-negative patients statistical analysis cannot be performed any more due to the low number of patients. This has been mentioned in the text. Within the OLT group we included all patients being anti-β/γ-positive or -negative, because there is evidence that the antibodies can even rise after transplantation. This has also been mentioned and discussed.

6. We agree and changed the discussion.

7. Data on antibodies to the different nuclear antigens in our patients were added and discussed.

8. This is a still unpublished preliminary observation.

We hope that we could meet the reviewers’ criticisms in an appropriate way.

With kind regards

Yours sincerely

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