Point- to Point- reply

Manuscript Number: 86907
Title: Acupuncture in diabetic peripheral neuropathy – neurological outcomes of the randomized ACUDPN trial

Dear editor, dear reviewers,

Thank you for your careful review and the comments and suggestions that we have taken on board and which have noticeably improved the manuscript once again. We would like to respond to the reviewers' comments as follows:

Reviewer 1

Reviewer 1: I think this is a very meaningful article, and the research design is relatively rigorous.

Authors: Thank you for your positive feedback.

Reviewer 1: I have some suggestions for the author's reference: 1.The reference format in the main text needs to be modified

Authors: We have modified the references according to the journal´s guidelines for authors.

Reviewer 1: 2.Detailed reasons for patient being excluded during the initial screening process should be provided.

Authors: Thank you for the remark. We added the information in the results section in chapter 3: " the main reason was that the required pathological nerve conduction velocity was not met or nerve conduction was in the normal age range; one patient was excluded because of very severe neuropathy with atrophy of the proximal leg muscles."

Reviewer 1: 3.A small sample size may limit the research results and statistical validity.

Authors : Thank you for the remark. The explanation of the smaller sample size with the consequences for the statistical analysis was provided in the result section in line 175 ff page 5. We added a sentence in the "limitations" section of the discussion on page 11, line 290: The sample was smaller than initially planned, a bigger trial would be useful. The statistical analysis was adapted accordingly.

Reviewer 1: 4.The outcome evaluator blind should be considered due to selectivity bias.

Author: Thank you for the remark. Yes, we completely agree, a blinded assessor would reduce the bias. We had addressed the point in the limitation section of the discussion on page 11 line 294 in the original manuscript: Due to limited resources the clinical, assessments could not be performed through a blinded assessor.

Another sentence was written in the section "further research": "Future trials should be conducted with a sham-control group and proper blinding."

Reviewer 1: 5.In theory, both ITT analysis and FAS analysis should be considered. I would like to know the reason why the author did not conduct ITT analysis.

Authors: Thank you, we agree. The analysis has been conducted with the FAS and the ITT but only for the primary endpoint, which has been published elsewhere. We have modified the sentence in the section on statistical analysis on page 5, line 166: "Analysis f the primary endpoint was performed with the full analysis set (FAS) based on an intention-to-treat principle, the results have been published elsewhere [19]."

Reviewer 16. It difficult to understand why the sample size calculation resulted in a data of 110 patients, while we only included 62 patients.

Authors: Thank you – we sadly had to end the trial recruitment prematurely because of the SARS-CoV2 pandemic and restrictions in research. We have mentioned this at the end of the section on statistical analysis on page 5 in line 175: "The trial was terminated prematurely due to strong restrictions on research with direct patient contact caused by the COVID-19 pandemic. Consequently, the previously calculated sample was not reached. Due to the lower sample size, the study center was not included as fixed effect in the statistical models for primary and secondary endpoints in the predefined statistical analysis plan. Instead, study center was included as a random effect in the analyses."

Reviewer 2

Reviewer 2: This study is not-blinded open study. The number of patients was small. However, this research has worth to publish.

Authors: Thank you for your positive feedback.

Reviewer 3

Reviewer 3: After reviewing your manuscript, in my opinion, the Figure 2 of the manuscript is not clear enough in detail. I suggest that the time nodes for the two groups to receive the intervention and evaluate the outcome should be indicated in the flow chart.

Authors: Thank you for your remark. We have modified figure 2 and added more details regarding time points and follow-up's.