Author’s response to reviews

Title: Outcome of MS relapses in the era of disease-modifying therapy

Authors:

Muriel Stoppe (muriel.stoppe@medizin.uni-leipzig.de)

Maria Busch (maria.busch@medizin.uni-leipzig.de)

Luise Krizek (Luise.Krizek@medizin.uni-leipzig.de)

Florian Then Bergh (thenberf@medizin.uni-leipzig.de)

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Author’s response to reviews:

Dear Dr Lou,

thank you for your email message as of Jan 06, 2017. We would like to acknowledge the effort taken by yourself and the reviewer, resulting in the encouraging and detailed comments on our manuscript.

Please find enclosed a modified version of the manuscript. We would like to explain below how we addressed the reviewer’s suggestions.

Reviewer #1:

This is a manuscript by Stoppe et al … I was really excited to get to read this manuscript and while this is an important report, there are some deficits that should be addressed as outlined below.

1. Figure 2: The figure legend and figure layout require some extra attention. For example, I did not understand the "treatment" bars for each section. In primary relapse treatment, does the
"treatment" bar mean that most of them had already reached partial remission at the time of their first visit before IVMP? I'm sure the authors wish to convey something else there than what it looks like. I am interpreting the "outcome" bar to mean the evaluation after the patients had received IVMP. Also, the gray cone of 23.7% that leads into the escalating relapse treatment bar…I have no idea what that is there for. The most informative part of the figure was the "outcome" bar for each patient classification area, but the percentage values are not included in the figure which would be helpful.

Authors’ response: Figure 2 and its legend were revised. We split the bars representing the number of patients with an indication for treatment and those actually receiving treatment; in addition, we deleted the cone and added the percentages of treatment outcomes.

2. The SPMS patients should be removed as there are not sufficient numbers for comparison. The authors could mention in the discussion the outcome for these patients since the "n" is small.

Authors’ response: The reviewer is certainly correct when stating that the number of SPMS patients would be far too small for a comparison of treatment effects in SPMS vs RRMS. This was not the intention of the study, but rather collecting all relapses in one year, regardless of the course of disease (CIS, RRMS or SPMS). Postulating that relapse outcome is comparable among these groups, and since the small number of SPMS patients could potentially introduce only a minor bias, we would like to keep these patients part of the analysis.

3. Discussion Page 11 Lines 259-262. This paragraph is comparing the current data to historical findings. It should be expanded with MUCH more detail so that it is clear how this project is similar and distinct from the historical findings. Also, there is confusion regarding references 19 and 20, since the authors first post that response rates were 50-80% (line 260), and then 40% in the next sentence (line 262) while referencing the same papers. This needs to be fixed.

Authors’ response: As suggested, the discussion was expanded. Reference 19 states different recovery rates, depending on the time of follow-up; both figures are cited, once for a follow-up time of seven or 28 days, respectively. The text has been adapted accordingly.

4. Finally, since most DMTs impact the immune response, a paragraph regarding the known effects of MP on the immune system should be included in the Introduction and discussed in the context of why relapse response may have been so small in the follow-up.
Authors´ response: A paragraph referring to the mechanism of MP has been added to the discussion.

We feel that the additions and adaptations have helped to improve our manuscript, and, again would like to acknowledge the constructive attitude the reviewer has displayed.

Sincerely,

Prof. Dr. Florian Then Bergh
Consultant Neurologist
Neuroimmunology