Author's response to reviews

Title: The effect of scheduled antibody testing on treatment patterns in interferon-treated patients with multiple sclerosis

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Author's response to reviews: see over
Mr. Jhonell De Los Santos

BMC Neurology

RE: MS: 5533027271124522

Dear Mr. De Los Santos:

On behalf of my co-authors, we thank you for forwarding your reviewers’ comments on our paper entitled “The effect of scheduled antibody testing on treatment patterns in interferon-treated patients with multiple sclerosis.” I have indicated below how we have responded to each of the comments, which are highlighted for easy identification in the manuscript.

**Reviewer 1:**

The main flaw of the study, as … reported by the Authors, is the imbalance of the number of visits between the two groups, as it is well known that a more frequent neurological examination allows a detection of a higher number of relapses and, as a consequence, a higher number of change of treatment. The number of visit is not reported in the manuscript and it must be added.

The number of study visits was provided in the Methods section on page 4 but has now been expanded for clarity.

It is also not reported if the patients are aware they are enrolled in a study in which Nabs are quantified every three months and that the presence of NABs can impact efficacy of IFNB treatment. The role of patient willing in change of treatment is not considered, or not clearly specified.

Investigators or designees explained the study procedures, risks, and potential benefits, if any. Patients reviewed the study instructions and informed consent form and were given the time and opportunity to have any questions concerning the conduct of the study answered to their satisfaction. This expanded statement has been substituted on page 4 for the single sentence about informed consent previously included.

The impact of Nabs on clinical /MRI activity was not included, correctly, among the outcomes of the study, but the authors should also underline that the presence of NABs / BABs was associated with higher number of relapses and/or MRI activity in comparison with Nabs negative patients, as reported in the two
subgroups of patients scheduled for Nabs quantification (table 3).

The reviewer’s query actually pertains to Table 4. We have added a sentence to better describe the content of this table on page 9 (first paragraph).

A sentence should also focus on the number of visits or contacts with MS clinic per years MS patients have in real world setting, independently from performing or not Nabs test. The data of this study show that a contact every three months with a MS clinic for performing a blood test (not clear with or without a neurological evaluation) is able to detect a double number of relapses in comparison with the usual schedule (table 2).

Studies suggest that in the real-world setting, MS patients may have as many as 8 all-cause physician visits per year [Asche CV, Singer ME, Jhaveri M, Chung H, Miller A. All-cause health care utilization and costs associated with newly diagnosed multiple sclerosis in the United States. J Manag Care Pharm. 2010;16(9): 703-712.


Thank you for pointing this out: we have added a sentence about this, and cited Giovannoni et al, in the Limitations section on page 10.


We now describe this paper in the Discussion section on pages 9-10. Thank you for the suggestion.
Reviewer #2

Someone may note that different modified ITT criteria were introduced for patients in different groups. As a result, more patients were excluded from analysis in the "usual care" arm (n=95) compared to the "Ab testing" arm (n=33) (Figure 1). Would final results change if analysis is done using the identical criteria for two groups (e.g., all patients not lost to follow up)? This is an important question that needs to be addressed.

Given the fact that our study was quite large, had a high rate of completion, and that all time points were analyzed in both arms, we believe that whether the mITT criteria or other criteria had been used would not have affected the endpoint of change in therapy by the 12-month time point, which was statistically significant. We have commented on this on page 10 in the first Discussion paragraph.

Did "Ab testing" patients have more frequent evaluations by their neurologists compared to "usual care" patients? Could more frequent visits (time spent with a patient) also impact treatment change initiated by a physician? This issue can be raised in the Discussion section.

This is an important question, but we believe that we have already addressed it in the following sentence at the bottom of page 10: “Another consideration when interpreting the results is the imbalance in clinic visits that the Ab testing arm would have received versus the usual treatment arm, which could have affected management choices irrespective of Ab results.”

We thank your reviewers for their helpful comments and for their complimentary evaluations of our study, which I have not included here. We will be pleased to respond to any further comments or queries and look forward to publication of our paper in your journal.

Yours truly,

Edward Fox, MD, PhD