Author's response to reviews

Title: Prognostic implications of a carefully performed neurological assessment in patients with a first event suggestive of multiple sclerosis

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Version: 4 Date: 17 February 2009

Author's response to reviews:

Amsterdam, Feb 17 2009

Dear madam, sir,

Please find resubmitted the paper: prognostic implications of a carefully performed neurological assessment in patients with a first event suggestive of multiple sclerosis after it has been adapted to the recommendations of the reviewers.

The changes consist in the following:

According to reviewer 1:

· In figure 1 and 2 the number of patients ‘at risk’ for each study period, for the two comparison groups are now also given.

· The Cox proportional hazard models used to estimate interaction are now reported in full.

According to reviewer 2:

1. The requested work (Polman et al, J Neurol 2008 Apr: 255(4):480-7) has been referenced in the second paragraph of the discussion.

2. The conclusion of the abstract has been reworded; in combination with MRI
has been added.

3. A sentence about MRI sequences and administration of Gd has been added.

4. The software used for statistical analysis has been added to the patients and methods section.

5. In answer to question no 5: There was no difference in the average number of enhancing lesions between the mono and multifocal groups at baseline (median 0 [IQR 0-1] in the monofocal and median 0 [IQR 0-1] in the multifocal group) and yes there was a difference between the average number of T1 lesions in the monofocal (median 1 [IQR 0-4]) and in the multifocal group (median 2 [IQR 0-6]). This isn’t mentioned explicitly in the present paper, because it was already thoroughly discussed in the former paper (ref no 8).

6. As suggested the first 2 paragraphs under the section entitled ‘Comparison of the impact of MRI findings at screening, month 3, month 6 on time to CDMS etc.’ have been reworded.

7. Please find additional table 4 which was refered to in the last section of the results but was not attached has now been attached.

8. The last sentence of the 4th paragraph of the discussion has been reworded and the word trend is no longer used.

9. The title has been changed to: MRI characteristics are predictive for CDMS in monofocal, but not in multifocal patients with a clinically isolated syndrome.

Minor Essential Revisions reviewer 2:

Abstract:

1. Background; first sentence has been revised, ‘and time’ is now included.

2. Methods: multi – and then monofocal has been changed in mono- and multifocal.

Introduction:

3. Page 5, reference (2) is no longer superscripted.

4. The last sentence has been reworded to ‘..period of the BENEFIT study’ as suggested.

Patients and Methods:

Study design, patients and procedures:

5. Second paragraph, third sentence: MRI has been changed to MRI findings, as this is indeed what is meant with MRI here.

6. Third paragraph, page 7: International Panel has been changed to IP as
suggested.

7. Fourth paragraph, first sentence has been changed to ‘In the case of…’

Statistical Analyses:

8. First paragraph, page 8, has been changed to ‘…versus by symptoms only.’

9. Second paragraph, page 9: the explanation of CSF has been removed

Results:

10. First paragraph, third sentence, page 10 has been changed to ‘..and 176 received placebo’

11. Reference to figure 1: 1a,b has been changed to 1A,B.

12. The section entitled: ‘Comparison of key baseline characteristics’ the first sentence as been changed as suggested. to ‘symptoms, while 100 (45%) presented by signs..’.

In addition to these changes I would like to point out two errors I came across while doublechecking all data. It concerns the section ‘Comparison of the impact of MRI results…: in the 6th line the p value concerning the hazard ratio comparing monofocal patients with and without at least one gado enhancing lesion at month 3 should be 0.002 instead of 0.001 and in the 15th line the p value concerning the hazard ration comparing multifocal patients with and without at least one gado enhancing lesion at month 6 should be 0.11 instead of 0.36. None of these changes has an impact on the conclusions and the text is not essentially changed, but they were not correct in the previous version of the paper.

I hope the manuscript as such has been sufficiently changed as to be published, in case it is not, we'll be happy to address further comments,

Best wishes,

Jessica Nielsen,