Reviewer’s report

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

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Reviewer: Alessandra Solari

Reviewer’s report:

The manuscript is a post-hoc analysis of data from the BNEFIT study, a RCT assessing the effectiveness of interferon beta-1b in clinically isolated syndrome (CIS) patients.

The authors had two main objectives:

1. To compare key baseline characteristics of CIS patients with mono- or multifocal clinical presentation;
2. To assess the influence of mono- or multifocal clinical presentation on time to clinically definite multiple sclerosis (CDMS) over a two-year period.

The second and more relevant objective was assessed in the placebo arm (176 CIS patients). Overall, clinical presentation did NOT affect time to CDMS. However, subgroup analyses revealed an influence of clinical presentation on time to CDMS stratifying by MRI lesion load and Gd enhancement at baseline (T2 lesions < 9 vs. # 9; Gd present); and by Gd enhancement at 3 and 6 months.

Post-hoc analyses are by definition not pre-specified and potentially unlimited, yielding results that can be misleading because of multiple comparisons (and false positive findings). This limitation is clearly recognized by the authors (see discussion section). To improve the informativeness of the study I recommend the following:

1. In Figures 1 and 2 (Kaplan-Meier curves), the number of patients “at risk” for each study period, for the two comparison groups should be given.
2. The Cox proportional-odds models used to estimate interaction should be reported in full, providing number of CIS, CDMS, hazard ratios and 95% confidence intervals for each independent variable.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests: 
I declare that I have no competing interests
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