The authors report on 141 patients with multiple sclerosis (MS) that were assessed retrospectively longitudinally in order to associate clinical responsiveness to development of neutralizing antibodies (NABs) to interferon beta (IFNb) therapy.

Patients are stratified a priori into three groups; those with active, relapsing disease (A); those with sustained progression of disability (B); and those with stable, inactive MS during follow-up (C). NABs are analysed by the cytopathic effect assay and report if positive once.

The authors find significantly smaller proportions of NABs positive patients in the stable disease group. However, even in the active groups (A, B) the proportion of NABs positive patients is only 17 %.

The authors conclude that there may be either a sampling error as NABs were only measured once or NABs may not be the reason for clinical irresponsiveness.

The topic of the paper and its findings are clearly of interest. However, several issues require clarification:

• It is somewhat difficult to comprehend how often the patients were assessed clinically and by NABs testing. The authors may consider producing a figure with the timeline.

• This figure could substitute figure 1A that does not add any information not presented in the main text body already.

• It should also be clarified how long patients were on IFNb before NABs testing, and whether relapses were only counted if occurred within 6 months of initiation of IFNb therapy (as per definition in the Methods section). If this is the case, there clearly is a sample bias, and it cannot be concluded that NABs are only present in a minority of clinically active patients.

• In this respect it surprises that mean disease duration was 11 years. The authors are encouraged to also how long patients had been treatment naïve before entering this study.

• Standard deviations rather than standard errors of mean should be reported.

• The discussion would be benefitted from focussing on the results and could be
condensed.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

my department has received, with approval by the rector (president) of heinrich-heine-university unrestricted research grants from bayerscheringpharma, biogenidec, merckserono and teva for research into the pathogenesis, prevalence and impact of neutralizing antibodies to ifnß.

i have received personal compensation, with approval by the rector of heinrich-heine -university for consulting and speaking on multiple sclerosis-related and neuroimmunological topics from the above companies.