DOES THE PRESENCE OF NABS AGAINST IFNS NECESSITATE A SWITCH TO ANOTHER CLASS OF THERAPY? – NO

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In this debate with my honorable colleague Dr Pier Sorensen, I will support the point of view that the presence of neutralizing antibodies should not be by and in itself sufficient to discontinue treatment with interferons.
I will develop the following points:
1) A series of technical issues have rendered the field rather muddy –or foggy: determining the limit for positivity; determining at which levels Nabs become biologically relevant; determining at which levels Nabs become clinically relevant i.e. low versus high; cross-reactivity of antibodies i.e. can one use one single antigen to measure antibodies generated by 3 different products
2) How to appreciate clinical effect on a group basis? 30% - 40% reduction in relapse rate means even when that even when treatment is fully effective patients will continue to have relapses-indeed less but still some! How long does effect remain once drug stopped (or loses efficacy due to High Nabs?); Patients who end-up having high NABs generally (in 3 trials) start by having more beneficial effect of IFN; UBC experience
3) How to appreciate clinical effect on a group basis? Or better: How to reconcile Evidence Based Medecine and the questions posed by the one single patient sitting in front of me? 3 examples of difficulties in decision-making despite being in the optimal situation in individual patients for which clinical, Gad-MRI, NAbs levels and MxA induction data are available; Should one use the “optimization scheme” developed by Canadians? Should one add one set of data, The NAB results?
4) Different Interferon behave differently: Beta-1b: high frequency of NAB +, generally lower levels and faster cycling through towards disappearance; Beta-1a: low frequency of NAB+, generally higher levels and slower return to an antibody negative status; This can be explained by differences among the IgG subclasses making the NABs. This, in turn is explained by differences in glycosilation of the proteins on one hand and by the differences in the properties if IgG subclasses on the other hand
5) Could there be other ways Interferon act than by binding to their receptor? MS is the only condition where injections of the antigen have been continued when high levels of antibodies have been attained. This create an hyperimmune state against the antigen; I am not yet sure of the mechanism of action of Glatiramer Acetate, however I am sure that this is another situation where Antigen continues to be injected in the presence of high levels of antibodies; Is there a clue there? Could immune complexes be involved? This could explain some of the remaining effect once NABs have appeared; We will show long term effect
6) The MS neurologist is basically a physician and as such the following rules of thumb should apply: Do not try to fix what does not need fixing: if the patient is doing well do not change the treatment; Try and understand the pathogenesis of the problem: If a patient appears not to do well, do MRI with Gad and measure NABs, then decide what should be done; Try and generate data through randomized trials to determine what is the best way of handling the problem at hand.
My conclusion: I would not stop interferon just because there are antibodies present. I would clinically assess patients and make decision once I have all the elements: Clinical course, Gad-MRI, Nabs and MxA induction.