

Medical Update Memo

March 3, 2010

Clinical effect of neutralizing antibodies to interferon beta that persist long after cessation of therapy for multiple sclerosis

Summary

Interferon beta (IFN β) is a first-line treatment for people with MS. However, increasing evidence suggests that the presence of neutralising antibodies during treatment is associated with a reduction in treatment efficacy. The authors of this study found that anti-IFN β neutralising antibodies could persist after treatment cessation and were associated with higher disease activity and poorer clinical outcome. **Arch Neurol. 2010 Feb 8**

This retrospective study aimed to confirm that neutralizing antibodies (NAb) to interferon beta can persist after therapy withdrawal and to evaluate whether persisting NAb are associated with a worse clinical disease course in multiple sclerosis (MS).

The group studied consisted of a total of 71 patients with relapsing-remitting multiple sclerosis treated with interferon beta in the past. Persisting NAb after therapy withdrawal were tested using the cytopathic effect assay.

Patients with and without persisting NAb were compared on several outcomes: the change in annualized relapse rate from prior to interferon beta treatment initiation to after cessation of treatment, time to sustained disability on the Kurtzke Expanded Disability Status Scale, and the use of disease-modifying treatments after cessation of treatment with interferon beta.

Seventeen of 71 patients (24%) tested NAb positive after a median interval of 25 months (interquartile range, 10-51 months) after interferon beta treatment cessation. Eleven of these 17 patients (15%) were high-titer NAb positive (>150 10-fold reduction units per mL). Persisting NAb were associated with an increase in the annualized relapse rate ($P = .04$) and a reduction in time to reach a sustained Expanded Disability Status Scale score of 6.0, ie, the need for unilateral assistance to walk 100 m ($P = .02$). Moreover, NAb-positive patients were treated with second-line therapy significantly more often, especially mitoxantrone ($P = .006$).

CONCLUSION: Anti-interferon beta NAb can persist after interferon beta treatment withdrawal and are associated with overt clinical disease activity. This is suggested by an increase in relapse rate and faster disability progression and is supported by the observed

need for more aggressive therapy after interferon beta treatment cessation. Prospective studies are warranted to confirm these results.

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