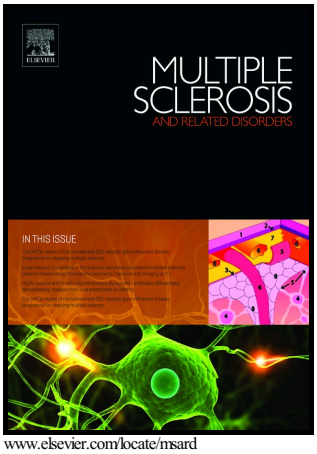

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Re-evaluating the Incidence of Natalizumab-Associated Progressive Multifocal Leukoencephalopathy

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Abstract

Objective

To estimate the prospective risk of developing PML during therapy with natalizumab in JCV-seropositive patients.

Methods

We analyzed postmarketing data about the incidence of PML on natalizumab and quantified the risks by either applying the Kaplan-Meier estimator or, where this was not possible due to the unavailability of the respective raw data, using formulae yielding very similar figures.

Results

In JCV-seropositive patients with prior immunosuppressive treatment, the PML risk for months 25–48 of natalizumab therapy is about 19.5 per thousand. Without previous exposure to immunosuppressants, the risk during months 25–48 is approximately 7.4 per thousand, and for months 49–72, it is approximately 10.8 per thousand. If one additionally assumes that the JCV index is in the range 0.9–1.5, then the incidence for months 49–72 is around 6.2 per thousand in comparison to 17.0 per thousand when the JCV index exceeds 1.5.

Conclusions

Biogen's statistics concerning the risk of PML on natalizumab treatment, while in principle helpful, underestimate the true incidence systematically and significantly. Realistic estimates of the longterm risk are nearly double those previously published, with some patient groups carrying a risk that is almost nine times higher. Fortunately, a refined risk-stratification algorithm with the incorporation of such measures as L-selectin and CSF lipid-specific antibodies has the potential to make natalizumab a considerably safer drug.