CORRESPONDENCE

Natalizumab and Progressive Multifocal Leukoencephalopathy

THE BRIEF REPORTS ON NATALIZUMAB WERE REFERRED TO BIOGEN IDEC, THE MANUFACTURER, WHICH OFFERS THE FOLLOWING RESPONSE: After learning of one confirmed and one suspected case of progressive multifocal leukoencephalopathy (PML) in patients treated with natalizumab, Biogen Idec and Elan quickly notified the Food and Drug Administration (FDA) and other regulatory authorities. We worked closely with the FDA to understand the significance of these findings and to determine the appropriate action. On February 28, we voluntarily suspended all dosing and marketing of natalizumab; swift and decisive action was guided by our commitment to patient safety. Immediate efforts also included a comprehensive review of all adverse events to search for unrecognized occurrences of PML. We identified as suspicious a report of malignant astrocytoma and requested a reevaluation. The case was subsequently confirmed to be PML.[1]

The review of data on these patients, who are described in this issue of the *Journal*,[1-3] is part of a larger analysis under way in consultation with regulatory authorities and the National Institutes of Health (NIH) to assess the risk of PML in natalizumab-treated patients. An independent panel with expertise in the diagnosis and management of PML is reviewing all suspicious and ambiguous findings to evaluate them for possible PML. A better understanding of the risk of PML will be possible only once the evaluation is complete. We hope to share findings from this evaluation by the end of the summer.

Unfortunately, we know little about PML and JC virus, but important observations can be gleaned from these case reports. One report suggests that clinical PML may be preceded by JC viremia.[1] Another demonstrates that PML is not uniformly fatal.[2] It is possible that testing for the appearance of JC virus in plasma, along with a high degree of clinical suspicion, will permit early diagnosis and discontinuation of natalizumab therapy and allow patients to recover. Similar findings have been reported for BK virus, a related polyomavirus that infects transplant recipients.[4]

Multiple sclerosis is a serious and disabling neurologic disease with limited therapeutic options. Since the suspension of natalizumab, we have heard expressions of frustration and disappointment from patients and others in the multiple sclerosis community. We understand that for many, natalizumab provided new hope for the management of this difficult disease; given these events and the efficacy and otherwise good safety profile of natalizumab, the importance of better defining potential risks of its use will be key to understanding its place in therapeutics.

We thank patients, physicians, and the entire multiple sclerosis community for their continued patience and support during the past few months. We remain firmly committed to a thorough evaluation of the safety profile of natalizumab so that we may provide physicians and patients with the necessary information to make informed benefit–risk decisions about their multiple sclerosis therapy.

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