Viral- and myelin-specific cellular immune response in MS patients treated with natalizumab: a cross-sectional and a longitudinal study

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INTRODUCTION:

Natalizumab (Tysabri) is a monoclonal antibody which binds to the α4 integrin, molecules that are expressed on the surface of activated lymphocytes and allow them to cross the blood-brain barrier. By preventing the rolling and diapedesis of CNS auto-antigen activated lymphocytes, this medication has been shown to be highly efficient in decreasing the relapse rate and the progression of disability in multiple sclerosis (MS) patients (1,2). However, since its approval, eight MS patients treated with natalizumab suffered from progressive multifocal leukoencephalopathy (PML), on a total of approximately 57,000 treated patients (as of end of May 09). PML is a severe demyelinating disease of the central nervous system. The polyomavirus JC (JCV) infects 60-85% of the normal adult population (3-4), and its reactivation in the setting of immuno-suppression leads to a lytic infection of oligodendrocytes (3). Yet, since the blood cell counts are not decreased and since it does not seem to be associated with other opportunistic infections, natalizumab cannot be considered as a classical immunosuppressant. Therefore, other mechanisms have to be looked for.

In this ongoing cross-sectional and longitudinal study, we examine the JCV activity in the peripheral blood of Tysabri-treated patients over a one-year period. Using RT-PCR specific for JCV, we are determining their JCV DNA load in different compartments. At the same time-points, we are assessing the cellular immune response against JCV as well as against other viruses used as controls (EBV and CMV) and against the myelin oligodendrocyte glycoprotein (MOG), a recognized target in the CNS. We compare these responses with a cohort of patients treated with IFN-β.

Increased proliferation and IFN-γ secretion of JCV-specific T cells in the blood of MS patients on natalizumab

**CONCLUSION:**

\[\text{There is no increase of the JCV viral load in MS patients on natalizumab over time. These data confirm those from others (6).} \]

\[\text{However, there is an enhancement of the JCV-specific cellular immune response after 9-12 months of treatment, as assessed by proliferation and ELISPOT assays. By contrast, the responses against the control viruses (EBV and CMV) or against the myelin antigen MOG remain unchanged.} \]

\[\text{Contrasting with patients on natalizumab, there is no increase of the JCV-specific cellular immune response in patients on IFN-β.} \]

REFERENCES:


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