

Anti-JC-virus antibody prevalence in a German MS cohort

Dear Sir,

The anti-JC-virus-IgG (anti-JCV) antibody status has been introduced to stratify patients with multiple sclerosis (MS) treated with natalizumab for the risk of developing progressive multifocal leukoencephalopathy (PML). We tested sera of 511 patients (360 females, 151 males) from 9 German MS centres for the anti-JCV antibody status applying the published protocol.¹ The samples were either taken for the purpose of treatment decision making (e.g. treatment discontinuation, treatment initiation with natalizumab) or within the prospective German natalizumab pharmacovigilance study after obtaining written informed consent. This study was approved by the local ethical committees at the different sites.

The overall seroprevalence in our German cohort was 56%, and there was no significant sex difference (females 55%, males 58%, Figure 1A). The seropositivity rate gradually increased with age, from 37% in patients younger than 20 years to 77% in patients at the age of 60 years or beyond (Figure 1B). Our data independently confirm the published data in other cohorts, applying the same methodology.^{1,2} The observed increase in seropositivity with age, fitting a reported annual seroconversion rate for anti-JCV-antibody status ranging between 2% and 3%,¹ strongly argues for a close clinical and serological follow-up of patients tested negative for anti-JCV antibodies when applying the test to stratify patients for the risk of developing PML in clinical practice.

In addition, we studied six patients with PML from our cohort prior to ($n = 3$) or at the time of PML diagnosis ($n = 3$). All of these patients tested positive for anti-JCV antibodies. All non-PML patients with detectable JCV-DNA in serum (1 of 33 tested) or urine (3 of 18 tested) also tested positive for anti-JCV antibodies, supporting the potential utility of this method: no false-negative results were observed. However, no firm conclusions, such as risk calculations, can be drawn from these data as the number of patients with PML included was too low. Long-term observational studies are on the way to prospectively correlate the JCV antibody positivity and the development of PML

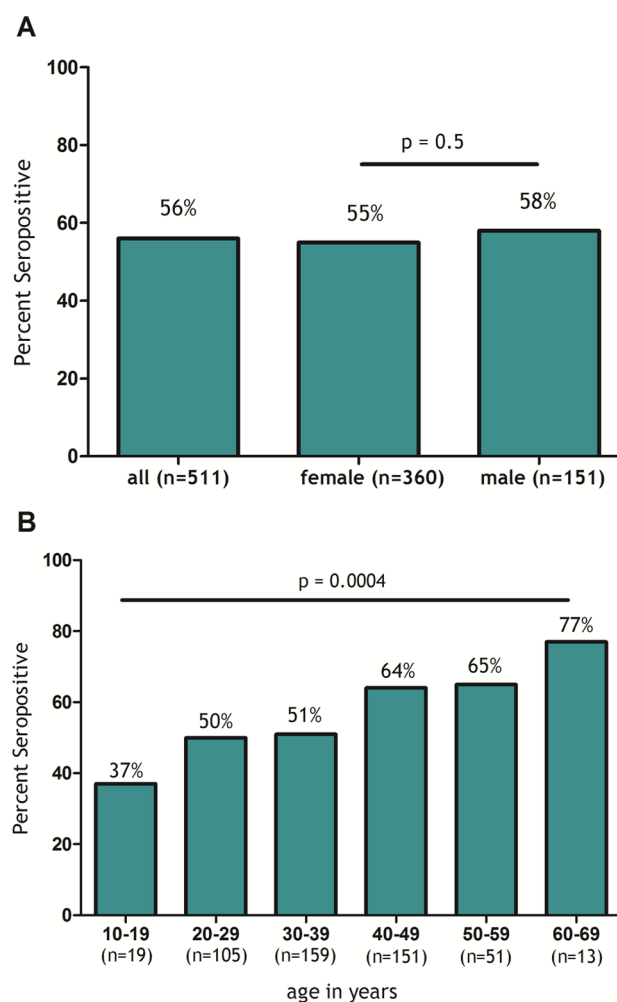


Figure 1. (A) The frequency for anti-JCV antibodies in all patients, and separately for male and female patients. The chi-square test demonstrated no significant sex difference ($p = 0.5$). (B) The positivity rate for anti-JCV antibodies for different age groups of 498 of 511 patients with data on age at sampling available. The chi-square test for trend demonstrated a significant increase with age ($p = 0.0004$).

during treatment with natalizumab.³ In the meantime the test might already be a useful tool to assist in treatment decisions in a proportion of patients.⁴ Nevertheless, high clinical and paraclinical vigilance for signs of severe

adverse effects such as PML will still be mandatory when treating patients with MS with highly immuno-active compounds such as natalizumab, regardless of the test result for anti-JCV antibodies.

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Conflict of interest

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