Shift from fingolimod to alemtuzumab: what happens next?

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Background: A particularly high reactivation of MS has been reported in patients who received alemtuzumab after fingolimod, in particular when a short washout between the two treatments occurred.[1,2] We aimed to understand whether this shift enhances the risk for MS reactivation, or if such possible reactivation has simply to be expected when a treatment is changed due to inefficacy.
Methods: Subjects with relapsing-MS, shifting from fingolimod to alemtuzumab due to inefficacy and referring to 11 Italian MS centers were enrolled. We collected the following clinical and demographic data: age; gender; age at onset; relapse before, during and after fingolimod (during washout period and during alemtuzumab treatment); time to first relapse during washout and alemtuzumab treatment; new T2/Gd enhancing lesions in the last brain MRI during fingolimod and in the first one during alemtuzumab; number of lymphocytes at alemtuzumab start.
Results: We enrolled 77 patients (age: 38 years (SD:9.7); 20-66 years; females: 61(79%), disease duration: 13.7 years (7.3)). 37 patients received more than one course of alemtuzumab. The ARR during fingolimod was 0.60 (SD:0.76), during washout 1.33 (SD:2.34), after alemtuzumab 0.20 (SD:0.46). After alemtuzumab, seven patients experienced one relapse, and two subjects two relapses. The median time to first relapse during washout was 28 days, while after the initiation of alemtuzumab315 days. We did not observe drop-outs from alemtuzumab.
The last MRI during fingolimod showed new T2 and Gd enhancing lesions in 45/65 (69.2%) and 34/58 (58.6%) patients, respectively. The first MRI during alemtuzumab showed new T2 and Gd enhancing lesions in 5/48 (10.4%) and in 1/46(2.2%) patients. Mean washout period was 2.7 (SD:2.7) months. Before alemtuzumab start, lymphocyte count was: < 0.5 x 10^3/mL in 10/53(18.9%) patients; 0.5-< 0.8 in 10(18.9%); 0.8-1.0 in 4(7.5); and >1.0 in 29(54.7).
Conclusions: In our cohort, alemtuzumab was able to dramatically reduce MS inflammation, both in terms of relapses and new T2/Gd enhancing lesions, as compared to the previous fingolimod treatment and the washout period. This was true despite washout and a normal lymphocyte count in about half of our cohort. Thus, a rapid initiation of alemtuzumab after fingolimod does not seem to be a risk factor for MS reactivation.
References:
1. Willis M, et al. NeurolNeuroimmunolNeuroinflamm. 2017
2. Huhn K, et al. J Neurol. 2018
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