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Disease activity after alemtuzumab correlates with specific patterns of immune reconstitution in individuals with multiple sclerosis

Objectives: To assess the changes in the absolute numbers of immune cells over the first 24 months post-treatment with alemtuzumab in multiple sclerosis (MS) patients and to correlate them with clinical and radiological responses. Materials and Methods: A single-center cohort of 26 patients with relapsing remitting MS treated with alemtuzumab. Patients underwent clinical evaluation and blood sampling every three months, and MRI every six months. Absolute and relative numbers of B, T and natural killer (NK) cells were evaluated by conventional flow cytometry over the first year post treatment. In order to measure the proportion of effector and regulatory T-, B- and NK-cell subsets over treatment, a highly standardized method for flow cytometry was employed in a subset of 12 patients. Statistical analysis: a linear mixed model analysis was applied to assess whether immune reconstitution correlated with clinical/MRI responses. Results: Responder patients have an increased proportion of NK cells and a decreased proportion of CD3+ T cells in the first six months of treatment, compared to non-responders (mixed effect analysis, p= 0.027 for T cells and p= 0.025 for NK cells). Analysis of reconstitution of NK cells over the first year of treatment demonstrated a persistent increase in the proportion of CD56bright NK cells over the first 6 and 12 months of follow up (p= 0.04 at month 6). We observed an overall decrease in the proportion of memory B cells (p=0.01 at month 6 and p=0.02 at month 12) and an increase in the regulatory phenotype (p=0.03 at month 1 and p=0.04 at month 3). Conclusion: Alemtuzumab expands regulatory NK and B cell subsets. Responders vs non responders have differential T- and NK cell reconstitution. Further experiments are ongoing to expand the sample with the analysis of cell subpopulations of the 26 patients enrolled.