Should we consider immune reconstitution for patients with more active MS? No

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In this debate, I will briefly discuss the word “consider” and the notion of (more) active MS before focusing more on the immune reconstitution (IR), defined as re-building of the immune system after a global depletion. Depletion of specific cell populations e.g. B cells, will not be addressed in detail. IR is what happens to the immune system when recovering from global depletion. Contemporary MS treatments relevant in this context are alemtuzumab, cladribine, and haematopoietic stem cell transplantation (HSCT). IR mechanisms are diverse, and vary between treatments. Reconstitution after HSCT occurs by increased thymic output and naïve lymphocytes, while homeostatic proliferation with increased effector memory cells and a relatively reduced thymic output characterizes reconstitution after alemtuzumab. This explains the high frequency of secondary autoimmunity after alemtuzumab. IR has both positive and negative consequences. The latter include risk of infections and secondary autoimmunity. Despite great hopes HSCT offers, there is no class I evidence for its efficacy and it is currently not recommended outside of properly designed trials in specialized centres. Cladribine, a “pulsed” IR offers promise but the mechanisms of IR and safety are not fully known. IR may be dangerous in MS even without systemic immune suppression. Severe inflammatory rebound after stopping natalizumab or fingolimod can trigger IR inflammatory syndrome (IRIS). Indiscriminate offering of drastic immunosuppression followed by IR to any patient with more active disease should be avoided.