

## Targeting Immune Dysregulation: Evolution of IRT



**Mark S. Freedman, MSc, MD,  
FANA, FAAN, FRCPC**

Senior Scientist, Neuroscience  
Program  
Ottawa Hospital Research  
Institute  
Professor of Medicine,  
Neurology  
University of Ottawa  
Director, MS Research Unit,  
Neurology  
Ottawa Hospital – General  
Campus  
Ottawa, Ontario

The treatment landscape for multiple sclerosis (MS) has evolved substantially over the past couple of decades along with our better understanding of the disease process. The goal has always been to target the part of the immune system (the adaptive immune system) mistakenly attacking the CNS while sparing that which protects or repairs the body (the innate immune system). The immunomodulators were the first to show the ability to do this, and although the efficacy was modest, the safety was significant. With the evolution of higher efficacy agents also came great toxicity or trade-offs. These usually took the form of emergence of opportunistic infections, since the immune

system was being compromised by the constant need to maintain the therapies. The latest round of agents has become known as immune reconstitution therapies (IRT), owing to their ability to enact a treatment response after only a short exposure and maintain the response without the need for constant administration. The durable response from just 1-2 courses of these agents can last for years.

IRT have several advantages over the maintenance therapies: there is no need for constant immune suppression that leads to more opportunistic infections; the reconstitution phase does not impede the potential immune cells capable of repair; they offer long-term durability without the need for re-treatment for years, ideal for pregnancy; vaccinations may still be possible. At least two new therapies, alemtuzumab and cladribine qualify as IRT and both are given similarly once a year for 2 years with the possibility of re-treatment with a single course should this be needed in the future. The result is a safer, yet more efficacious cell-depleting therapy that does not impair immune surveillance and allows for repair cells to work unimpeded. Should disease recur in the future, a short course of these same agents is all that may be necessary.