The future of NMO treatment is immune tolerance, not immunosuppression.

A. Jacob

NMOSD has seen a rapid evolution in the last 2 decades. All aspects of the condition particularly defining the disease, characterising underlying pathophysiology/autoantibodies and development of new drugs have advanced very quickly. In fact in the last 6 months, 3 phase 4 clinical trials have reported positive results and are set to revolutionise treatment. This is a remarkable and unique achievement for a rare disease. As in other autoimmune diseases most of the treatment modalities are immunosuppressive (e.g. azathioprine, mycophenolate, rituximab, eculizumab, satralizumab, ineblizumab) with risk of side effects particularly infections and cancers. In contrast to these strategies, inducing or restoring immune tolerance avoids these risks and effectively controls the disease. Vaccines against T cells, DNA, dendritic cells and strategies based on CAR T cells or T regulatory cells have the potential to induce lifelong remissions/cure without harm. However success in other autoimmune diseases (Type1 Diabetes, Multiple sclerosis) has been limited, perhaps because the inciting antigen or disease mechanisms are not well understood. AQP4 is undoubtedly the target antigen in majority of patients. Disease mechanisms in NMOSD are well understood. Does this offer a unique opportunity to attempt tolerisation? Should we focus our attention on effective targeted immunosuppression? Or can we tolerize ‘the enemy within’ to a friend. Will NMOSD lead us to the holy grail of autoimmunity?