

Anti B cell or non specific anti B+T therapy

Anti-B – yes

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More than a decade ago the dominant theories on the etiology and pathogenesis of MS revolved around a prime role of T cells that would recognize target autoantigens in the brain and orchestrate inflammatory insults on CNS parenchyma. Subsequently, numerous lines of research advanced robust evidence for a role of humoral autoimmunity and B lymphocytes in driving or contributing to the disease process. These included histopathological analyses of MS brains detecting immunoglobulin and complement deposits as well as B cells in lesions, and the retrieval of myelin-reactive antibodies and B cells in blood and CSF. The most convincing evidence came from therapeutic studies with the B cell depleting monoclonal anti-CD20 antibody rituximab in RRMS. This highly effective monoclonal induced early suppression of inflammatory disease activity. This temporal profile suggested an action on B cell function as antigen presenters and instructors of T cells rather than a modifying effect on autoantibody production. The clinical development of the humanized anti-CD 20 antibody ocrelizumab culminating in the two OPERA studies in RRMS completed last year replicated the marked therapeutic effects achieved with rituximab in the earlier phase 2 trial. Very interestingly, ocrelizumab also appeared effective in a recently completed phase 3 trial in PPMS. These results raise a number of questions as to the role of B cells in the pathogenesis of this disease type.

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