Title: Ofatumumab: A Novel Anti-CD20 Monoclonal Antibody for Multiple Sclerosis: A Review of Clinical Considerations

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Background: Multiple sclerosis (MS) is an antigen-specific, cell-mediated chronic autoimmune disease of the central nervous system (CNS). The disease is characterized by immune infiltration, progressive demyelination, and subsequent axonal loss, leading to a coterie of degenerative neurological symptoms, including, but not limited to, optic neuritis, partial myelitis, sensory disturbances, and internuclear ophthalmoplegia. While the exact inciting cause of the body's autoreactivity in MS is not fully understood, it is has been linked to genetic, environmental, and infectious factors. Among the FDA-approved medications for the treatment of relapsing–remitting multiple sclerosis (RRMS), such as interferon-β, glatiramer acetate, natalizumab, mitoxantrone, fingolimod, teriflunomide, and alemtuzumab, anti-B cell monoclonal antibodies (mAbs) show particular promise in decreasing relapses and diminishing neural inflammation, as measured by T1- or T2-gadolinium-enhanced MRI.

Methods – A literature review was conducted on NCBI's pubmed database of all known published clinical trials examining the use of ofatumumab (brand name kesimpta) for multiple sclerosis.

Results – Preliminary clinical trials have shown beneficial effects of ofatumumab in relapsing–remitting multiple sclerosis, such as reduction in new brain lesion formation on MRI, reduction in rates of clinical relapse, and prolonged duration of efficacy with no evidence of rebound activity after stopping the treatment. Furthermore, a favorable safety profile has been noted [1]. High-dose, intravenous ofatumumab used as an RRMS treatment in phase II randomized, double blind placebo-controlled trial has shown no serious adverse effects, with decreased relapse incidence relative to placebo observed (19% vs. 25%) [2]. In phase II, placebo controlled, randomized, manufacturer-sponsored MIRROR study, the effects of varying doses of subcutaneous ofatumumab in patients with RRMS were measured through the rate of new gadolinium-enhancing T1 brain lesions detected via MRI [3]. Patients were divided into groups of differing medication dosages, including placebo, 3 mg, 30 mg, and 60 mg. A 65% reduction in the rate of new brain lesions was seen when comparing any of the ofatumumab-receiving groups to the placebo group, supporting the efficacy of subcutaneous ofatumumab [3]. Another systematic review of over 30 randomized controlled trials compared ofatumumab to other monoclonal antibody treatments available for RRMS, mainly analyzing the safety profiles of each drug [37]. No statistically significant difference was seen in the rate of infections among monoclonal antibody treatments used when compared to each other; however, compared to placebo, ofatumumab did have an increased risk of infection [4].

Conclusions:
In contrast to the more generalized immunosuppressive agents used for treating inflammatory stage RRMS, MoAbs-targeting CD20 cells have distinguished themselves in clinical trials for their ability to reduce symptoms on the Expanded Disability Status Scale (EDSS) and T2 gadolinium-enhanced MRI lesions. With the advent of ofatumumab, a subcutaneous, fully humanized anti-CD20 is now a treatment option for RRMS.

Citations

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