

MS Treatments and Their Mechanisms of Action

This entire article is aimed at providing a better understanding of the MS disease process, the disease-modifying therapies, and targets for treatment. The following chart lists the approved disease-modifying therapies for MS, and several (but not all) of the experimental drugs for MS in later-stage clinical trials, along with their mechanisms of action.

Much of the information was taken from MSAA's Summer 2009 issue of The Motivator, "MS Research Update 2009," by Dr. Diana M. Schneider. The full article may be viewed or downloaded by visiting www.msassociation.org, and then selecting "Publications," "The Motivator," and the "Summer 2009" issue. Readers without internet access may request a copy by calling MSAA at (800) 532-7667.

FDA-Approved Medications

Avonex® and Rebif® (both interferon beta-1a) as well as Betaseron® and Extavia® (both interferon beta-1b) reduce disease activity through a number of mechanisms, including the reduction of T cell inflammatory activity (Th1 cells). This reduces the number of T cells that damage myelin. They also stabilize the BBB, which helps to keep damaging cells out of the brain. The interferons also perform other positive actions as well.

Copaxone® (glatiramer acetate) is a mixture of four amino acids found in myelin basic protein, which is a key component of the myelin sheath that is damaged in MS. It diminishes several of the damaging MS disease processes, including the promotion of a shift in Th1 cells (pro-inflammatory) to Th2 (anti-inflammatory) responses. Copaxone increases T-regulatory cells that reduce immune system damage. It may also improve nerve function in the brain by increasing brain-derived neurotrophic factor (BDNF), which may provide neuroprotective effects.

Novantrone® (mitoxantrone) is an immunosuppressant that has been used for years to treat cancer. It targets rapidly dividing cells, including those believed to be involved in MS.

Tysabri® (natalizumab) is a laboratory-produced monoclonal antibody that prevents lymphocytes from migrating across the BBB and into the central nervous system (CNS). Recent data suggest that it may also enhance remyelination and stabilize damage to the myelin sheath. These and other results suggest that the drug may improve CNS function.

Experimental Monoclonal Antibody Medications

Campath® (alemtuzumab) is approved for the treatment of B-cell leukemia and targets T cells, B cells, and macrophages.

Rituxan® (rituximab) binds to a molecule on the surface of B cells and depletes them from the circulation.

Zenapax (daclizumab) is a genetically engineered antibody against a substance necessary for the growth of T cells. It results in a sustained but reversible reduction in activated T cells, and turns off inflammation.

Experimental Oral Medications

Cladribine causes a preferential and sustained depletion of specific classes of T cells in the immune system. It also reduces the overall T-cell inflammatory response.

Gilenia® (Fingolimod, FTY720) blocks potentially damaging T cells from leaving lymph nodes, lowering their number in the blood and tissues, including the CNS. It may reduce damage to nerves and enhance nerve repair. It also increases certain T-reg cells (which favorably regulate the immune system), and may promote a shift from Th1 (pro-inflammatory) to Th2 (anti-inflammatory) responses.

BG00012 (BG 12; fumarate; fumaric acid ester) may have a distinct dual mechanism of action. It modulates the immune system and has anti-inflammatory properties, as well as reduces the damaging macrophage activity. It may also have neuroprotective effects. This is due to its activation of a substance that increases the resistance to cellular damage from what is termed "oxidative stress."

Laquinimod modulates the immune system and is an anti-inflammatory agent. From animal studies, it reduces infiltration of macrophages and CD4+ cells across the BBB and into the CNS. It also promotes a shift from Th1 (pro-inflammatory) to Th2 (anti-inflammatory) responses.

Teriflunomide modulates the immune system by reducing the division of harmful T cells. It disrupts the DNA of rapidly dividing cells, which results in antiproliferative effects.

Statins are oral medications most commonly prescribed to lower cholesterol. Their anti-inflammatory properties have stimulated more clinical trials in MS.

Additional Therapies Being Studied

Tovaxin® is a T-cell vaccine where T cells are removed from a small amount of the patient's blood and then are grown in a test tube environment (where they increase in number). These T cells are inactivated, and then injected back into the patient. As a result, the immune system is stimulated to recognize and eliminate the inactivated cells as well as active damaging cells.

BHT-3009 is a DNA "vaccine" containing a gene for myelin basic protein (MBP). The vaccine coats the MBP and induces immune system tolerance. This action limits the response of specific damaging immune cells involved with MS, thereby reducing the attack against the MBP in MS patients.

Vitamin D3 studies show that an inverse relationship appears to exist between vitamin D3 levels and the probability of developing MS. Proteins activated by vitamin D bind to and alter the function of a section of the chromosome near a specific gene variant which increases the risk of MS, suggesting that vitamin D deficiency during pregnancy might alter the function of fetal genes.

Tetracycline Antibiotics including minocycline and doxycycline, have immunomodulatory and neuroprotective activities. They also appear to decrease the passage of leukocytes across the blood-brain barrier.