

Immune Suppressants and Related Drugs

ROBERT S. KATZ, M.D.

Rheumatology Associates, Inc.

Associate Professor of Medicine, Rush Medical College

Chicago, Illinois



Foundation of America, Inc.



Imuran, Cytoxan and Related Drugs

Although immunosuppressive drugs can have serious side effects, they can be of great value in the treatment of lupus. They may help to prolong life, preserve kidney function, reduce symptoms, and sometimes serve to put the disease into remission. These drugs help to reduce damage to vital organs, such as the kidneys and lungs.

Steroids used alone to treat major organ involvement in lupus must sometimes be given in high doses. This increases the risk of short-term and long-term side effects, which may sometimes be worse than the disease itself. Immunosuppressive drugs can be used either in addition to, or instead of, steroids to spare the patient some of the undesirable side effects of steroid therapy.

Thus, immunosuppressive and cytotoxic drugs are used in the treatment of systemic lupus erythematosus (SLE) for two major reasons: They are potent drugs which help to control disease activity in major organs, including the kidney, brain, cardiovascular system, and lungs. Also, they may reduce or eliminate the need for steroids (cortisone derivatives such as prednisone).

How Do They Work?

Cells in the body divide and grow at varying rates. Examples of rapidly dividing cells include the antibody-producing cells of the immune system; blood cells; hair cells; and gonadal (sex) cells. Cytotoxic (cyto=cell, toxic=damage) drugs work by targeting these cells which grow at a rapid rate.

In lupus, the immune system produces auto-antibodies at a rapid rate of growth. Cytotoxic medicines can suppress the cells involved in the hyperactive immune response.

There are risks associated with the use of cytotoxic drugs. The immune system may be suppressed too much, which causes an increased susceptibility to infection, particularly shingles (a painful, blistering skin condition) and pneumonia. The bone marrow can be suppressed as well, which results in reductions in red blood cells, white blood cells, or clot-forming platelets. Suppression of hair cell growth may lead to overall loss of hair. The cytotoxic effects on gonadal cells can lead to sterility.



Imuran

(GENERIC NAME: AZATHIOPRINE)

Imuran is less potent and less effective than Cytoxan, but has fewer side effects. It can produce nausea. Its use may cause the white blood cell count, platelet count, or red blood cell count to decrease. With long-term use, Imuran also might increase the risk of developing lymphoma (cancer involving the lymph glands, liver and spleen). However, it is well tolerated in most cases.

Blood tests to determine the white blood cell, platelet, and red blood cell count should be done regularly in patients receiving this drug. Adjustments in dosage are made if the tests indicate a serious decrease in blood counts.


Imuran is steroid-sparing and studies have shown that it clearly improves liver and kidney lupus.

Cytoxan

(GENERIC NAME: CYCLOPHOSPHAMIDE)

Cytosxan is well tolerated by most patients. Like Imuran, it may cause an upset stomach and its use may decrease the white blood cell count, platelet count, or red blood cell count. Blood tests to determine these blood counts should be done regularly for those receiving Cytoxan. If the blood count is seriously decreased, the dosage is adjusted and the blood counts will generally return toward normal.

Patients on long-term Cytoxan have an increased risk of developing malignancies, including leukemia and bladder cancer. Cytoxan may also cause temporary or permanent sterility in both women and men, preventing them from having children. It may also lead to damage of a developing fetus if a woman gets pregnant while being treated with the drug. Cytoxan can cause bleeding from the bladder; this usually can be prevented by drinking large amounts of water. Cytoxan predisposes a patient to develop shingles. It also can cause hair loss. Like Imuran, the use of Cytoxan may predispose a person to develop unusual infections, particularly when it is given in combination with high doses of steroids.



Cytoxan can be given as oral tablets, but more often is given through the vein (intravenously, or IV). This procedure generally takes between 15 and 60 minutes. Large amounts of intravenous fluids are also given to dilute the concentration of Cytoxan in the bladder. Pre-medication for nausea is sometimes given, but treatment with Cytoxan is generally well tolerated.

IV Cytoxan seems to be associated with fewer malignancies and many fewer bladder problems, while being equally effective. Controlled studies also show that it improves kidney and autoimmune lung disease.

Related Drugs

Leukeran (generic name: **chlorambucil**) and Mustargen (generic name: **nitrogen mustard**) are two cytotoxic drugs related to cyclophosphamide. Both have similar side effects to Cytoxan.

Methotrexate is usually given orally on a weekly basis, although it may be given by injection. The dosage is generally 7.5 to 25 milligrams per week. Methotrexate is well tolerated by most patients. Its use in lupus has not been thoroughly tested, but it is given commonly for rheumatoid arthritis and has been shown to produce improvement of joint pain and stiffness. It is only modestly effective for organ-threatening lupus. Liver disease and lung reactions can occasionally occur with the use of methotrexate. Blood counts and blood liver enzyme tests should be monitored regularly in patients receiving this drug, and the dosage modified if side effects are detected.

CellCept (generic name: **mycophenolate mofetil**) and **Neoral** (generic name: **cyclosporine**) are two medications that modify the immune system, which, in lupus, appears to be both overactive and misdirected. Both of these medications are used to prevent rejection of the donated organ in kidney, liver, heart and lung transplants. CellCept can cause nausea and diarrhea. Cyclosporin may elevate blood pressure and reduce kidney function.



Conclusion

All of these agents are steroid-sparing. While cytotoxic medications should not be used in cases of mild lupus, these medications can be very helpful and even life-saving when major organs are involved, or in cases where the lupus is quite active and symptomatic. Sometimes a kidney biopsy or other tissue biopsy is necessary before deciding whether to use these drugs. Even in more serious cases of major organ involvement, cytotoxic drugs should not be used indefinitely without good reason.

It is important to weigh the beneficial effects as well as the risks involved in cytotoxic drug therapy. Doctors use the term "risk-benefit ratio" to describe the comparison of side effects to beneficial effects of medication. While these cytotoxic drugs are not FDA-approved for use in SLE, they are commonly used and accepted as standard practice. People with lupus should discuss the risk-benefit ratio of these medications with their physician.



The Lupus Foundation of America

The Lupus Foundation of America (LFA) was established in 1977 to educate and support those affected by lupus and find the cure. The LFA supports research, education, awareness, patient services, and advocacy.

The Lupus Foundation of America is the only nationwide organization exclusively serving individuals, families and friends affected by lupus. The LFA has hundreds of local chapters and support groups throughout the United States, as well as international affiliates around the world.

The LFA is a grassroots, volunteer-driven organization. Contact the LFA or the chapter that serves your area to find out how you can become involved in our mission.

For information about lupus or to locate the chapter nearest you, visit our website at www.lupus.org or call toll-free 1-800-558-0121.

Become a Lupus E-Advocate and help pass federal legislation that will benefit people with lupus. Send an e-mail message to advocacy@lupus.org and enter SUBSCRIBE in the subject line. You'll receive periodic advocacy updates and other breaking lupus news and information.



Lupus Foundation of Illinois
20 E. Jackson Blvd., Suite 1150
Chicago, Illinois 60604
312.542.0002