

## *Cancer Therapy May Offer New Hope to People with Lupus*

Researchers at Johns Hopkins report success in using high doses of the anti-cancer drug cyclophosphamide to treat patients with moderate and severe forms of lupus, a chronic and sometimes fatal autoimmune disease. Their findings are published in the January 10, 2003 issue of *Arthritis and Rheumatism*.

In the study, by a team at Johns Hopkins' Lupus Center and Kimmel Cancer Center, 14 patients with lupus underwent four days of high-dose intravenous cyclophosphamide. All had failed to respond to standard disease therapies and endured significant organ failure. After an average follow-up of more than two and a half years, five patients had complete responses and three of those patients have remained disease-free after completely discontinuing treatment. Six patients achieved a partial response and take lower doses of previously ineffective immune-suppressing drugs. Two patients did not respond to therapy, and one patient had some response but developed new renal disease.

"Living with long-term severe lupus is devastating, as the body's immune system attacks itself," says Michelle Petri, M.D., professor of rheumatology at Johns Hopkins. "Lupus has permanently damaged one or more organ systems in about half of all our patients, in spite of currently available therapies."

"The idea with this treatment is to blast the lupus once and wipe out the abnormal immune system," says Petri, "and allow the body to relearn and function normally without further therapy."

In lupus, a patient's immune cells incorrectly initiate reactions against tissues and organs, causing progressive damage. Investigators believe "reprogramming" the immune system could be an effective way of treating such disorders.

"Stem cells—the bone marrow cells that give rise to all immune cells—are resistant to high-dose cyclophosphamide," says Robert Brodsky, M.D., associate professor of oncology and medicine. "The malfunctioning immune cells are destroyed by the cyclophosphamide, while the stem cells withstand the therapy and continue to rebuild a new, hopefully disease-free immune system."

Studies at other institutions are using a similar high-dose cyclophosphamide regimen, but also include a bone marrow or stem cell transplantation. Because high doses of cyclophosphamide are toxic to the bone marrow, some investigators collect and re-infuse a portion of the patient's bone marrow and/or stem cells following treatment to quickly repopulate the marrow destroyed by treatment. Brodsky and Petri believe transplantation is unnecessary, because the cyclophosphamide-resistant stem cells repopulate the marrow anyway. In addition, they worry that transplantation may reintroduce diseased immune cells into the patient.

Standard therapy for moderate and severe lupus is a monthly lower dose of cyclophosphamide, but after six months, only about 25 percent of lupus patients fully respond, reports Petri. Patients who fail standard treatment after six months can continue monthly cyclophosphamide regimens, but experience significant side effects, including ovarian failure, severe osteoporosis, hypertension and infections from the cyclophosphamide and high doses of steroids to control inflammation. In the current study of high-dose cyclophosphamide, patients had no premature ovarian failure, and all 11 pre-menopausal patients maintained menses. Side effects were hair loss, nausea and a brief period of low blood cell counts.

A larger, randomized trial of high-dose cyclophosphamide without stem cell transplantation versus standard therapy for organ-threatening active lupus is under way at the Johns Hopkins Lupus Center. For more information, contact the Lupus Center at 410-614-1573 or [stdman@jhmi.edu](mailto:stdman@jhmi.edu).

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