

# New Therapy Gives Leukemia Patients Another Chance for Survival

**A** new therapy for treating leukemia patients who have relapsed after chemotherapy and bone marrow transplantation is offering these patients an exciting new treatment option, and may improve their long-term survival.

The pioneering treatment combines donor lymphocyte infusions to fight leukemia with gene therapy to combat serious complications from the procedure. Society researcher Richard Burt, M.D., director of the allogeneic bone marrow transplant program at Northwestern Memorial Hospital in Chicago, developed the new treatment funded by a \$216,000 translational research grant from the Leukemia Society of America.

Dr. Burt treats patients who have relapsed with infusions of lymphocytes—a form of white blood cells—collected from the blood of the original marrow donor. Infusions of the immune-surveillant white blood cells produce a desired immune response which kills the leukemia cells that cause a relapse. While the donor lymphocytes are intended to attack the leukemia cells and destroy them, they also may attack the tissues in the body, a reaction known as graft-versus-host disease.

“Graft-versus-host disease can be minor. In fact, physicians prefer that leukemia patients have a small level of the disease because that signals a strong attack against leukemia,” says Dr. Burt. “However, if it is severe, it can be fatal. Because of this possibly severe complication, researchers have developed a method to destroy the lymphocytes if they begin to cause a severe case of graft-versus-host disease.”

To control graft-versus-host disease, researchers place a gene from the Herpes simplex virus, called thymidine kinase gene (TK gene), into the donor lympho-



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cytes before the donor cells are infused into the patient. Cells with the TK gene can be killed with ganciclovir, a drug developed to treat Herpes simplex and also used extensively to fight infection after bone marrow transplantation.

To mark the cells carrying the TK gene, researchers also attach a harmless bacterial gene to the donor lymphocytes. Researchers can then determine, through laboratory techniques, which lymphocytes are carrying the TK gene. Physicians then transfuse only those lymphocytes armed with the TK gene into patients.

When transfused into a patient, the lymphocytes kill leukemia cells, but in some cases they attack normal tissues and cause graft-versus-host disease. As part of the new procedure, physicians would give patients ganciclovir injections for five to 21 days to fight severe or extensive graft versus host disease. “When the ganciclovir is given to the patient, the lymphocytes containing the TK gene

produce harmful substances within themselves that cause disease cells to die. Normal cells are not expected to be injured because they do not have this TK gene,” says Dr. Burt.

Because the treatment selectively destroys leukemia cells, without harming the patient’s healthy population of blood cells, it can be repeated a number of times if necessary. “It’s a treatment that is technically difficult and very labor intensive, but it’s an easier treatment for patients to undergo than chemotherapy or transplantation,” says Dr. Burt. “Much like a blood transfusion, patients can be treated mostly in the clinic. Patients do not have to stay in the hospital or recuperate for months. Their lives are not interrupted and they can continue work and other regular routines.”

Dr. Burt believes this is the first time donor lymphocyte infusions have been combined with gene therapy to treat leukemia patients in this country. Based on results in small numbers of leukemia patients at Northwestern University and in France and Italy, he is optimistic that this new therapy will be effective in both preventing leukemia relapse and treating graft versus host disease. In the future, the gene therapy might be combined with bone marrow transplants to treat patients even earlier in the course of their disease.

A collaborative research effort with Northwestern Memorial Hospital and the Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Iowa Methodist Medical Center in Des Moines, and the Cancer Center of the Medical College of Wisconsin in Milwaukee will extend the treatment to more U. S. patients with other malignant diseases, such as lymphoma, Hodgkin’s disease, myeloma, and myelodysplastic syndrome. **ML**