

Researchers at the University of Nebraska Medical Center are studying a new approach to bone marrow transplantation that they hope will revolutionize certain cancer transplants. Through a study, they are testing the safety and effectiveness of the so-called "mini-transplant" in adults with leukemia or lymphoma.

The mini-transplant, which is rapidly being accepted and studied at transplant centers around the country, is performed as an outpatient therapy with significantly less toxicity than with a traditional allogeneic bone marrow transplant. Allogeneic transplants are transplants that use bone marrow from related and unrelated donors to create a new, cancer-free immune system in the patient.

**A POTENTIALLY REVOLUTIONIZING therapy** UNMC's approach to the mini-transplant will involve using a familiar cancer drug —

pentostatin — with a new twist, said Steven Pavletic, M.D., UNMC oncologist and associate professor

**RESEARCH**

by Vicky Cerino

of internal medicine. Dr. Pavletic and Greg Bociek, M.D., UNMC oncologist and assistant professor of internal medicine, are principal investigators of the study.

"Pentostatin plays an important role in suppressing the patient's immune cells during the transplant process. There's a lot of interest in pentostatin nationwide," Dr. Pavletic said. The drug will be used in combination with doses of radiation six times smaller than a traditional transplant, as well as a very gentle form of chemotherapy, Dr. Pavletic said. Because of its mildness, mini-transplants are expected to reduce the risk and side effects of graft-versus-host disease — a potentially fatal side effect of allogeneic transplants.

"Our protocol is designed to be very non-aggressive," Dr. Pavletic said.

Half of the patients in the study will receive allogeneic bone marrow transplant therapy from related donors such as relatives, and the other half will receive bone marrow from unrelated donors through the National Bone Marrow Registry.

Some of the enrolled patients have responded to other standard treatments, but their disease is at a high risk of coming back. Other patients are older than 60, can't tolerate high doses of radiation and chemotherapy, or their cancer has returned after an autologous stem cell transplant.

"We use this therapy with patients who otherwise have very little hope. Instead of no chance for survival, we hope we can achieve a 30 to 50 percent cure rate. We want to find something for these patients," Dr. Pavletic said.

The transplantation process is a delicate balance of trying to suppress the patient's immune system while trying to prevent the patient's body from rejecting the donor bone marrow cells and contracting graft-versus-host disease.

The theory behind traditional allogeneic bone marrow transplantation is to give patients high doses of radiation and chemotherapy, wipe out the bone marrow, wipe out the disease in the bone marrow, and wipe out the immune system to "create space" to infuse the donor's bone marrow cells into the patient, Dr. Pavletic said.

"The theory then is that the donor's bone marrow will engraft or become part of the patient," Dr. Pavletic said. "Then you have no leukemia and you are cured. With time, what we learned, is that it's not as simple as this."

Researchers think the success of the mini-transplant lies in what's called "graft-versus-leukemia effect." Dr. Pavletic said he and his colleagues have learned that donor cells are probably the most critical part of therapy.

"The idea for this study was born here in our center from our expertise — based on our experience in transplantation and on new developments and knowledge," Dr. Pavletic said.

The UNMC/NHS transplant program is recognized internationally for its expertise in the diagnosis and treatment of leukemia and lymphoma, and is one of the busiest bone marrow and stem cell transplant centers in the world.

James Armitage, M.D., started the program in 1982 with the UNMC Lymphoma Study Group.

"I think this is where transplants are going," he said. "There is a lot to be learned but the initial promise is so clear. I think the approach of doing high-dose radiation and chemotherapy is going to be eliminated with time — probably three to five years from now. We want all this horrible toxicity associated with allogeneic transplantation eliminated."

"The mini-transplant is rapidly being accepted by transplant physicians. I truly think it's going to revolutionize the allogeneic transplantation field. Our expectations are high, and I think the patients' expectations should be high too."

Dr. Pavletic said there are many new anti-cancer drug discoveries steadily making cancer therapy easier and more efficient for patients. For progress to continue, Dr. Pavletic said patients are needed to enroll in clinical studies. Only 3 percent of patients typically enroll in clinical trials. "Clinical trials are the only way we can quickly obtain the information we need on new drugs and treatments," he said.

One example of rapid approval by the U.S. Food and Drug Administration took place May 10, 2001 when it granted Novartis Pharmaceuticals Corp. approval for Gleevec™, an oral therapy for the treatment of patients with chronic myeloid leukemia in the accelerated or chronic phase after failure of interferon-alpha therapy. Dr. Pavletic was principal investigator of the UNMC portion of this national study.

"The approval of Gleevec™ in two years was the most rapid FDA approval ever," Dr. Pavletic said. "This is one of the reasons why it is important for patients to participate in clinical trials." *d*