

# Half-matched transplants widen pool of donors for leukemia and lymphoma

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Identifying a suitable donor for leukemia and lymphoma patients who need bone marrow transplants may be far easier now that results of two clinical trials show transplant results with half-matched bone marrow or umbilical cord blood are comparable to fully matched tissue, thanks in large part to the availability of effective antirejection drugs and special post-transplant chemotherapy. The finding means that nearly all patients in need of a transplant can find donors, according to Johns Hopkins scientists who participated in the trials.

Plans are under way for a four-year randomized trial for so-called haploidentical marrow or cord blood transplants in 380 patients to begin late this year or early next year. Many large medical centers, including Johns Hopkins, are expected to participate.

The results of the two studies are good news, Hopkins researchers say, because they address the problem faced by patients when no family members are a complete match for the patient's tissue type. Although patients and physicians may then seek donors through national registries, as many as half or more of patients looking for matches in these registries don't find one, and the search can take weeks to months.

During this time, a patient's disease can progress, notes bone marrow transplant expert Ephraim Fuchs, M.D., who adds that it is especially difficult for minorities to find matches because of their underrepresentation in national registries.

"People are dying waiting for matched donors from a registry," says Fuchs, associate professor of oncology at the Johns Hopkins Kimmel Cancer Center.

In the clinical trials, investigators from the Blood and Marrow Transplant Clinical Trials Network at 27 medical centers tested two types of transplants, those from half-matched (or haploidentical) bone marrow or cord blood, and published their results in the July 14 issue of *Blood*. Some 50 adult [leukemia](#) or [lymphoma](#) patients with advanced disease or at high risk for relapse were included in each of the Phase II trials. Six of the participating centers conducted both types of transplants. Johns Hopkins conducted the haploidentical transplant trial only.

Transplants with cord blood, collected from the umbilical cord and placenta after a baby is born, are generally done in children because of the small number of cells in a single unit of cord blood. Adults, on the other hand, need two units.

Bone marrow tissue is extracted by needle from the hip bone of donors. Marrow that is half-identical to a patient's tissue type can be obtained from parents, children and most siblings.

Results of the two trials show one-year survival rates of 54 percent for cord blood transplant and 62 percent for haploidentical marrow. Survival without disease progression at one year was 46 percent for cord blood and 48 percent for haploidentical marrow. The investigators say this is comparable to survival achieved by similar patients undergoing transplants from fully matched siblings or unrelated adult donors.

Relapse rate after one year was 45 percent for haploidentical marrow transplants and 31 percent for cord blood. No patients had severe graft versus host disease (GVHD) – an attack on the patient's normal tissues by immune cells of the donor -- after bone marrow transplant.

At one year, deaths not caused by relapse occurred in seven percent of haploidentical patients and 24 percent of cord blood transplants.

Fuchs says that in the past, haploidentical transplants failed more often because the transplanted cells caused severe GVHD, especially in older patients. Half of the patients enrolled in the current trials were 50 and older.

"Ten years ago, it was unthinkable to do a haploidentical transplant," says Fuchs, who led the haploidentical transplant clinical trial.

To overcome the GVHD problems, Fuchs and colleagues at the Johns Hopkins [Bone Marrow Transplant](#) Program pioneered the use of a [chemotherapy](#) drug called cyclophosphamide after the transplant to minimize the effects of GVHD. The drug wipes out the patient's immune system, leaving the transplanted blood stem cells intact. The stem cells create new disease-free blood cells in the patient.

The investigators also believe that a lower-intensity "conditioning" regimen of chemotherapy and radiation before the haploidentical marrow transplant may help prevent severe GVHD. The outpatient conditioning treatment lasts six days. Then, the donor's [bone marrow](#) is harvested and, that same day, infused intravenously into the patient. This is followed by two days of high-dose cyclophosphamide, and then, other immune-suppressing drugs.

Within 16 to 24 days, patients begin forming new blood cells including white blood cells and platelets, important for fighting infection and clotting blood. Thirty to 40 percent of patients are able to receive their transplants on an outpatient basis, but some patients are admitted for fevers or infections. Patients are monitored carefully and remain in proximity to the hospital for 60 days after the transplant.

Patients receiving cord blood transplants follow a similar regimen, but have seven days of pre-transplant chemo and radiation therapy and receive [cord blood](#) from two separate donors.

Fuchs anticipates that haploidentical [bone marrow transplants](#) may be tested more widely in nonmalignant diseases, such as aplastic anemia, lupus, and sickle cell anemia. Haploidentical [transplants](#) using post-transplant cyclophosphamide are being performed in medical centers outside of the U.S., including Italy, Thailand, Singapore, Israel, Australia, Belgium and England.

Provided by Johns Hopkins Medical Institutions

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