Transplant More Than Doubles Survival For Some Leukemia Patients

St. Jude Children's Research Hospital investigators reported markedly improved survival of pediatric patients transplanted for high-risk leukemia regardless of donor; cite treatment advances and better donor selection.

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Bone marrow transplant survival more than doubled in recent years for young, high-risk leukemia patients treated at St. Jude Children's Research Hospital, with patients who lacked genetically matched donors recording the most significant gains. The results are believed to be the best ever reported for leukemia patients who underwent bone marrow transplantation.

The findings are expected to make transplantation a treatment option for more children and adolescents with high-risk forms of acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) who lack genetically matched donors, either related or unrelated. The research appears in the July 14 edition of the scientific journal Blood.

"This study shows that transplantation offers real hope of survival to patients with high-risk leukemia that is not curable with intensive chemotherapy," said Wing Leung, M.D., Ph.D., the study's principal investigator and director of Bone Marrow Transplantation and Cellular Therapy at St. Jude. Leung linked the gains to advances in cancer treatment as well as improved infection control and more sophisticated donor selection.

Five years after transplantation, survival was 65 percent for the 37 St. Jude patients with high-risk ALL treated at the hospital between 2000 and 2007, compared to 28 percent for the 57 St. Jude ALL patients who underwent treatment between 1991 and 1999. ALL is the most common childhood cancer.

AML survival after transplantation rose from 34 percent for the 50 St. Jude patients treated between 1997 and 2002 to 74 percent for the 46 AML patients treated between 2002 and 2008.

During the same periods, there was an eight-fold reduction in infections, a four-fold drop in treatment-related toxicity and a 2.5-fold decrease in leukemia-related deaths. The overall survival gains coincided with an end to irradiation therapy for St. Jude leukemia patients, a treatment that is associated with a range of immediate and long-term side effects.

"We can now identify donors for virtually all pediatric patients who need transplant

to cure their leukemia. Importantly, our transplanted patients not only have high cure rates but also excellent quality of life, resulting largely from advances in chemotherapy, donor selection and supportive care," said Ching-Hon Pui, M.D., St. Jude Department of Oncology chair and the paper's senior author.

Bone marrow transplantation involves destroying the patients' own diseased blood-producing bone marrow and replacing it with hematopoietic cells from healthy donors. This study included three types of donors: genetically matched related donors; genetically matched unrelated donors; and partially genetically matched donors. Parents generally make up the third group, who are known as haploidentical donors.

The largest survival gains involved patients whose blood and immune systems were rebuilt with cells from haploidentical donors. Survival for these patients increased from 12 percent in earlier ALL and AML treatment eras to 88 percent in the most recent treatment era.

Historically, transplant patients fared best and suffered fewer complications when the donors were relatives who carried the same six proteins on their white blood cells. Known as HLA proteins, they serve as markers to help the immune system distinguish between an individual's healthy tissue and diseased cells that should be eliminated.

St. Jude investigators pioneered the use of haploidentical transplants, demonstrating that careful matching of patients and donors and proper processing of the hematopoietic donor cells enhances the anti-cancer effect of transplantation without significantly increasing side effects. The process involves careful testing and HLA screening of potential donors to identify the one whose immune system is likely to mount the most aggressive attack against remaining leukemia cells using specialized immune cells known as natural killer cells. The odds of finding a good haploidentical donor are 70 to 80 percent, compared to about a 25 percent chance of having a matched sibling donor, Leung said. The likelihood of finding a genetically identical, unrelated donor ranges from about 60 to 90 percent depending on the patient's race or ethnicity.

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